Human Subjects

Standard Operating Procedures

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1 Human Research Protection Program (HRPP)

1.1 Policy

The State University of New York at Stony Brook (University or Institution as used in this document) fosters a research environment that promotes the respect for the rights and welfare of individuals recruited for, and participating in, research conducted by or under the auspices of the University. In the review and conduct of research, actions by the University are 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*** often referred to as the Belmont Report. This includes researchers, research staff, IRB members, chairs and staff, the Institutional Official and any other employees engaged in human subject research. The actions of the University will also conform to all applicable federal, state, and local laws and regulations. In order to fulfill this policy, the University has established a human research protections program (HRPP).

Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice and the applicable regulatory requirements. The Stony Brook University Institutional Review Board (IRB) is registered with the Office of Human Research Protections and the Food and Drug Administration (FDA). The registration is updated regularly by the Institutional Official when changes are required or prior to the expiration of the registration.

1.2 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 timely and high quality education, review and monitoring of human research projects; and
- Facilitate excellence in human subject research.

The HRPP includes mechanisms to:

- Establish a formal process to monitor, evaluate and continually improve the protection of human research subjects;
- Dedicate resources sufficient to do so;
- Exercise oversight of research protection;
- Educate investigators and research staff about their ethical responsibility to protect research subjects; and

- When appropriate, intervene in research and respond directly to concerns of research subjects.

1.3 Institutional Authority

The University HRPP operates under the authority of the University Policy #P202R, "Research Involving Human Subjects," most recently revised and approved March 2019. 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…" The University Policy and these Standard Operating Procedures (SOPs) are available to all University investigators and research staff and posted on the Office of Research Compliance's website.

1.4 Ethical Principles

The University is committed to conducting research with the highest regard for the welfare of human subjects. It 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:

Respect for Persons, which is ensured by obtaining informed consent, consideration of privacy, confidentiality, and additional protections for vulnerable populations.

Beneficence, which is assured by ensuring that possible benefits are maximized and possible risks are minimized to all human subjects.

Justice, the equitable selection of subjects.

The University's Human Research Protection Program (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.

1.5 Definitions

Agent: all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility.

Common Rule: 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 Department of Health and Human Services (DHHS) regulations in 45 CFR 46 Subpart A. For the purposes of this document, references to the Common Rule will cite the DHHS regulations.

Clinical Trial: Per the Common Rule and NIH Policy, clinical trial means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes. FDA regulations refer to "clinical investigations" (see definition of "research" below).

Engagement: an institution is considered *engaged* in a research project when the involvement of their employees or agents in that project includes any of the following:

- Intervention for research purposes with any human subjects of the research by performing invasive or noninvasive procedures.
- Intervention for research purposes with any human subject of the research by manipulating the environment.
- Interaction for research purposes with any human subject of the research.
- Obtaining the informed consent of human subjects for the research.
- Obtaining for research purposes identifiable private information or identifiable biological specimens from any source for the research. In general, obtaining identifiable private information or identifiable specimens includes, but is not limited to:
- Observing or recording private behavior;
- Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided by another institution; and
- Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.

Human Subject (for research covered by the Common Rule, e.g., 45 CFR 46, etc.): A human subject as defined by the Common Rule is a **living** individual about whom an investigator conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. [45 CFR 46.102(e)(1)]

"Intervention" means both physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. [45 CFR 46.102(e)(2)]

"Interaction" means communication or interpersonal contact between investigator and subject. [45 CFR 46.102(e)(3)]

"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). [45 CFR 46.102(e)(4)]

"**Primary endpoint"** refers to an analyzed parameter (e.g., change from baseline at 6 weeks in mean depression scores).

"Secondary endpoint" refers to secondary objectives (e.g., a drug designed to prevent high blood pressure might also have a measure of whether quality of life is improved). A secondary endpoint always occurs with a primary endpoint.

"Identifiable private information" means private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information. [45 CFR 46.102(e)(5)]. Note: This definition is within the Common Rule. For a discussion of identifiability under HIPAA, please see Section 16.

"Identifiable biospecimen" means a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen [45 CFR 46.102(e)(6)]

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

Human Subject (for research covered by FDA regulations (21 CFR 50 and 56)): 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 a healthy human or may have a medical condition or disease. In the case of a medical device, a human subject/participant also includes any individual on whose tissue specimen an investigational device is used or tested (regardless of whether the specimens are identifiable). When medical device reserach involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human participants

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

Human Subject Research: any activity that meets the definition of "research" and involves "human subjects" as defined by either the Common Rule or Food and Drug Administration (FDA) regulations.

Institutional Official (IO): the person designated by the University to be responsible for the University's HRPP. The IO is legally authorized to represent the institution, is the signatory official for all Assurances, and assumes the obligations of the institution's Assurance. The IO is the point of contact for correspondence addressing human subjects research with OHRP, FDA, and other federal regulatory agencies. The Institutional Official follows the principals of the Belmont Report and all federal, state, and local regulatory requiments

Institutional Review Board (IRB): a board designated by the University to review, approve the initiation of, and to conduct periodic review of research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The IRB may be assigned other review functions as deemed appropriate by the University. All IRB members and Chairs are expected to abide by the ethical principles of the Belmont Report as well as all federal, state and local laws.

Research (Common Rule): a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge. For purposes of this part [the Common Rule], the following activities **are deemed not to be research:** (1) Scholarly and journalistic activities (e.g., oral hemployeeistory, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected. (2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters). (3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes. (4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions. [45 CFR 46.102(l)]

For the purposes of this policy, a **"systematic investigation"** is an activity that involves a prospective study plan that incorporates data collection and analysis, either quantitative or qualitative, 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)

Research (synonymous with **Clinical Investigation, Study - for activities under FDA jurisdiction):** 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 FDA under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act. This 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)] or any activity that evaluates the safety or effectiveness of a device. [21 CFR 812.2(a)], respectively; **or**
- Does not need to meet the requirements for prior submission to the FDA under these sections of the Federal Food, Drug, and Cosmetic Act, but the results are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. 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)]

Note: *Any activity in which results are being submitted to or held for inspection by FDA as part of an application for a research or marketing permit is considered to be FDA regulated research. [21 CFR 50.3(c), 21 CFR 56.102(c)]"*

Research under the Auspices of the University:
Includes research that:

- Engages this Institution in the activity, regardless of the location at which the activity is conducted;
- Is conducted by or under the direction of any employee or agent of this Institution (including students) in connection with his or her institutional responsibilities regardless of the location at which the research activity is conducted;
- Is conducted by, or under the direction of, any employee or agent of this Institution using any property or facility of this Institution, or involving the use of this Institution's non-public information to identify or contact human subjects.
- Research does not begin until the research has received all approvals required by the organization. The HRPP reviews the research in order to assure that all approvals have been obtained when applicable (e.g., conflict of interest, Radioactive Drug Research Committee, Human Radation Research Committee)

Test Article: Under the FDA regulations, covered test articles include:

Human Drugs: the primary intended use of the product is achieved through chemical action or by being metabolized by the body.

Drug: (a) substance recognized by an official pharmacopoeia or formulary; (b) substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; (c) substance (other

than food) intended to affect the structure or any function of the body; or (d) substance intended for use as a component of a medicine but not a device or a component, part or accessory of a device.

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

Medical Devices: "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is (a) recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them; (b) 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 (c) 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/C...

Biological Products: 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

Food Additives: in its broadest sense, a food additive is any substance added to food. Legally, the term refers to "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 characteristics of any food." This definition includes any substance used in the production, processing, treatment, packaging, transportation or storage of food.

Color Additives: 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.

Foods: dietary supplements that bear a nutrient content claim or a health claim.

Infant Formulas: liquid foods intended for infants, which substitute for mother's milk.

1.6 Regulatory Compliance

The HRPP is responsible for ensuring compliance with federal regulations, state law and institutional policies (including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe). All human subjects research at the University is conducted in accordance with the policy and regulations found in the Common Rule and 21 CFR 50 and 56.

Regulatory compliance for research funded by other federal agencies (e.g., Department of Defense, Department of Energy, Department of Education etc.) is addressed in the SOP Supplement: Additional Federal Criteria, as well as the Worksheet: Additional Federal Criteria to be used by IRB staff and members to ensure compliance with these specific regulations.

The University applies the International Conference on Harmonization ("ICH") Good Clinical Practices ("GCP") Guidelines (sometimes referred to as "ICH-GCP" or "E6") to research when required by a sponsor, and only to the extent that they are compatible with FDA and DHHS regulations.

The actions of the University will also conform to all other applicable federal, state, and local laws and regulations.

1.7 Federalwide Assurance (FWA)

The federal regulations require that federally funded human subjects research only be conducted at facilities covered by an FWA approved by the DHHS Office for Human Research Protections (OHRP). An FWA is an institution'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 Boards (IRBs) 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 has an OHRP-approved Federalwide Assurance (FWA# 00000125) and provides support to one on-site IRB. The HRPP also regularly utilizes the IRB services of Advarra (for industry-initiated, industry-funded protocols), and of the Pediatric and Adult Central IRBs of the National Cancer Institute (for certain cooperative oncology group protocols). Details concerning the process for using these external IRBs are available on the Office of Research Compliance website. Together, these five IRBs review all human research protocols conducted under the auspices of the University (unless the University enters into a reliance agreement to cede IRB

review to another outside reviewing entity, see section 1.14 for Multi-center research, and, e.g., via the SMART IRB Reliance Initiative (www.smartirb.org).

When human subjects research is not subject to the Common Rule or FDA regulations, SBU ensures that human research subjects benefit from equivalent protections by applying the Common Rule standards, with purposeful deviations that do not meaningfully diminish protections as noted within these SOPs.

Management of pre-existing Studies since the Revised Common Rule Went Into Effect

The revised Common Rule establishes that all studies approved, waived under .101(i), or determined exempt before January 21, 2019 is subject to the old rule through the close of study. All protocols approved or determined exempt on or after January 21, 2019 are subject to the new rule. Stony Brook University will not transition individual studies from the old to the new rule on or after that date.

1.8 Research Covered by the Human Research Protection Program

The University's HRPP covers all research involving human subjects that is under the auspices of the University. The research may be externally funded, funded from internal University sources, or conducted without direct funding.

1.9 Written Policies and Procedures

The University's 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 SBU IRB. This is not a static document. The policies and procedures are regularly amended by the Assistant Vice President for Research Compliance, in consultation with applicable institutional entities (e.g., Institutional Official (IO), Office of Research Compliance staff, Institutional Review Boards, University counsel, etc.). The IO will be kept apprised of all major revisions of the policies and procedures.

The Assistant Vice President for Research Compliance will keep the University research community apprised of new information that 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 University's Human Research website and copies will be available upon request. Information regarding updates to the policies and procedures are made available to researchers, research staff, IRB members and HRPP staff via informational sessions and email communications.

1.10 Human Research Protection Program Organization

The HRPP is a comprehensive system to ensure the protection of human subjects participating in research. It consists of various individuals, offices, and committees such as Institutional Official (IO), the Assistant Vice President for Research Compliance and Staff of the Office of Research Compliance (ORC), the Institutional Review Board (IRB), other committees or subcommittees addressing human subject protection (e.g., Institutional Biosafety Committee, Radiation Safety Officer, Radioactive Drug Research Committee, Conflict of Interest), investigators, research staff, and research pharmacy staff. The objective of this system is to assist the University 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 implementing the HRPP.

1.10.1 Institutional Official

The ultimate responsibility of the HRPP resides with the Vice President for Research (VPR). The Assistant Vice President for Research Compliance serves as the Institutional Official (IO) of the program. The IO is the primary contact at the University for the Office for Human Research Protections, Department of Health and Human Services, and the Food and Drug Administration. The IO, in close partnership with the Vice President for Research (see Section 1.11.1), has ultimate responsibility for oversight of:

- The development, management and evaluation of 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 all aspects of the HRPP program.
- The Institutional Review Board and University Investigators, ensuring that all are appropriately knowledgeable to conduct research in accordance with ethical standards and applicable regulations
- Keeping other appropriate institutional officials apprised on key matters regarding research at the University.
- Implementation the University's HRPP policy.
- Submission, implementation and maintenance of an approved FWA through the Department of Health and Human Services Office of Human Research Protection (OHRP).
- Assessment of the resources of the University's HRPP, including, but not limited to:

    - Staffing commensurate with the size and complexity of the research program;
    - Appropriate office space, meeting 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 noncompliance;

- Access to legal counsel; and
- Ensuring that the IRB, investigators, and staff receive training related to human research protections.

- Ensuring assistance for investigators in their efforts to carry out University's research mission.
- Development and implementation of needed improvements and ensuring follow-up of actions, as appropriate, for the purpose of managing risk in the research program.
- Development of training requirements as required and as appropriate for investigators, subcommittee members and research staff, and ensuring that training is completed on a timely basis.

1.10.2 University Counsel's Office

The University's HRPP relies on the University Counsel for the interpretation and application of New York State law and the laws of any other jurisdictions where research is conducted as they apply to human subject research.

1.10.3 The Investigator

The investigator is the ultimate protector of the human subjects who participate in research. The investigator is expected to abide by the highest ethical standards and to develop a protocol that incorporates the principles of the Belmont Report. He/she is expected to conduct research in accordance with the approved research protocol and to oversee all aspects of the research by providing supervision of support staff, including oversight of the informed consent process. All subjects must give informed consent (unless a waiver of informed consent is granted by the IRB) and the investigator must establish and maintain an open line of communication with all research subjects within his/her responsibility. In addition to complying with all the policies and standards of the governing regulatory bodies, the investigator must comply with institutional and administrative requirements for conducting research. The investigator is responsible for ensuring that all research staff complete appropriate training and must obtain all required approvals prior to initiating research. When investigational drugs or devices are used, the investigator is responsible for ceding oversight to the research pharmacy (for investigational drugs), or providing written procedures for their storage, security, dispensing and disposal.

1.10.4 Other Related Units

1.10.4.1 Office of Sponsored Programs (OSP)

The Office of Sponsored Program (OSP) staff review all research grants and agreements with federal, foundation, for-profit or non-profit sponsors. This institutional review ensures that all

terms of an award are in compliance with institutional and federal policies. Only designated individuals within OSP have the signature authority to approve and submit research proposals and to execute research grants and agreements on behalf of the University. As a further control, internal documents retained by OSP as part of the application process for extramural funding include information pertaining to IRB approval status, and investigator conflict of interest disclosure.

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, a subcontract is executed between the University 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. For unfunded collaborations, a subcontract is not executed, but OSP nonetheless verifies compliance by the other institution (e.g., copy of their IRB approval, etc.).

1.10.4.2 Pharmacy

Pharmacists from the Investigational Drug Service (IDS) within University's Hospital Pharmacy Department serve as consultants to, and/or IRB members on the IRB. They receive minutes from all IRB meetings and applicable correspondence from the University's off-site IRBs allowing the Pharmacy to have complete information about all IRB approved research that takes place at the University and under its jurisdiction. The Pharmacists assure that information about all studies involving drugs used in research is shared with the Pharmacy staff as appropriate. The University's Hospital Pharmacy and Therapeutics Committee is made aware of research involving drugs that is reviewed by the IRB.

The IDS controls the storage, dispensing, labeling and distribution of drugs used in human research conducted in the University Hospital, the Health Science Center, the Cancer Center, and the Ambulatory Surgery building. The IDS reviews and approves plans for the storage, dispensing, labeling, and distribution of drugs used in human research conducted in other campus sites. 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 participant, 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 participants.

If a patient admitted to the hospital as an inpatient is a subject in a research protocol involving medication, whether or not the study is conducted by the University, the Pharmacy must receive copies of all relevant study materials from the PI in order for the patient to continue the study

while an inpatient. The Pharmacy will review the protocol and accommodate the patient's continued participation in the study if deemed appropriate, after consultation with the Assistant Vice President for Research Compliance (and IRBs as applicable).

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

1.10.4.3 Office of Clinical Trials

The goals of this office are to streamline the process of industry sponsored clinical trials by utilizing the office as a single point of contact between industry sponsors and Stony Brook University Hospital. The functions of the Office of Clinical Trials are to:

- Match trials to appropriate investigators
- Help find resources for those investigators who lack support
- Review and/or create budgets for assessment and identification of study procedures, study visits, etc.
- Negotiate budgets with sponsors/Clinical Research Organizations
- Assist investigators with funding proposals, IRB, and regulatory submissions, if requested
- Collaborate with the Office of Sponsored Programs regarding CTA/Payment terms
- Collaborate with the Office of Grants Management regarding payments received.
- Advertise current studies enrolling subjects for recruitment purposes
- Track enrollment of subjects on Cerner/PowerTrials and OCT database
- Manage Clinical Trials Management System (CTMS)
- Provide Study Coordinator services, if requested.
- Mentor new investigators and study coordinators

1.10.5 Relationship among Components

The IRBs function independently of, but in coordination with, other University regulatory committees (e.g., legal office, Office of Grants and Contracts, Intellectual Property Partners and the Office of Sponsored Programs). IRB committees, however, make their independent determination whether to approve or disapprove a protocol based upon whether or not human subjects are adequately protected. The IRB has review jurisdiction over all research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency that has adopted the human subject regulations. Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of the University. However, those officials may NOT approve research if it has not been approved by the IRB.

Other areas represented for clinical trial research include Hospital Finance, Cancer Center, Office of Sponsored Programs, Office of Research Compliance, Office of Clinical Trials, Hospital Compliance, investigational pharmacy and others as deemed appropriate. The Office of Research Compliance reviews current research practices in order to assess effectiveness and propose improvements for the proper conduct and continued compliance of researchunder the auspices of the University.

Protocol-specific coordination: Submissions to the electronic management system for new and/or continuing studies must indicate University support, via appropriate, applicable electronic signature of delegated university officials for the following units and activities (as applicable), prior to commencement of the study:

- Pathology
- Pharmacy
- Radiology
- Privacy/Security
- Hospital Finance/Billing
- Chair of PI's department
- Use of research-related radiation
- Use of surgical pathology or cytology specimens

Note: electronic signature of PI and department chair must be present in order for the submission to be acted upon by ORC staff.

OSP and OCT staff have full administrative access to the electronic management system to assist in the coordination of various required institutional reviews and approval.

1.11 Human Research Protection Program Operations

In addition to the leadership structure described above, support staff members who dedicate 100% effort to the HRPP include, four (4) IRB Administrators and two (2) full-time IRB Assistants. See below for other individuals who contribute significant effort to the protection of human subjects at the University.

1.11.1 Assistant Vice President for Research Compliance (AVP-RC) and Staff of the Office of Research Compliance

The Office of Research Compliance (ORC), within the Office of Vice President for Research (OVPR), consists of an Assistant Vice President for Research Compliance (AVP-RC) and eight (8) staff. This office provides the primary administrative support for management of the University's HRPP.

Staff of the ORC report to, and are supervised by, the AVP-RC. For matters concerning the HRPP, the AVP-RC serves as the IO in administering general oversight of the HRPP and in the promulgation of the IO responsibilities detailed in 1.10.1.

The staff of ORC that is specific to SBU's HRPP consists ofindividuals responsible for facilitating all aspects of the IRB experience throughout the life of a research proposal involving human subjects. This responsibility includes the pre-review of documents and screening of research proposals prior to review by the IRB, assignment of reviewers, as well as serving as the liaison between the investigators and the IRBs. The IRB Administrators attend IRB meetings and help ensure proper documentation of discussions, including controverted discussions and actions taken by the IRBs during convened meetings. Each IRB Administrator serves as a voting IRB member on one of the two IRBs (and alternates for each other on the other IRB). These individuals either write, or oversee, the communication from the IRB to the investigator.

The IRB staff is always available to speak by phone or in person with investigators who need assistance in navigating any and all aspects of the IRB process. Individual consultations with the staff are particularly encouraged and strongly recommended for investigators of first-time submissions.

The structure of the Office of Research Compliance, with responsibility for the administrative support of multiple compliance committees, permits efficiencies and assurances that all relevant compliance approvals are obtained for a particular research activity.

The AVP-RC is the Human Protections Administrator per the FWA. Along with an Assistant Director, these staff members also have responsibilities in other areas of ORC, i.e., administration and management of the Institutional Animal Care and Use Committee, Institutional Biosafety- IBC (and DURC), Radioactive Drug Research (RDRC), and Stem Cell Research Oversight committees. The AVP-RC is also the Research Integrity Officer (RIO) and handles research misconduct allegations and proceedings for the University.

A Director of Research Security is responsible for Export Controls, Investigator COI, and assists with research misconduct allegations and proceedings,. This individual works closely with the QA IRB Administrator in handling COI involving human research.

1.11.2 Selection, Supervision and Evaluation of HRPP Supporting Staff

Selection Process: Policies and procedures of the Research Foundation of SUNY and SUNY, are followed for the recruitment and selection of HRPP professional and clerical staff. The University is an Affirmative Action/Equal Opportunity employer and educator. The University's hiring departments and the search committee assigned to each recruitment work together with Human

Resource's Recruitment, the Office of Diversity/Affirmative Action and the local Affirmative Action/Equal Employment Opportunity Committee to demonstrate the University's good faith efforts to locate and consider for employment a wide pool of applicants, including qualified persons of color, women, disabled persons and special disabled or Vietnam era veterans.

Depending on the position to be filled, variables to be considered in the selection of HRPP staff include prior experience in IRB administration or another position within an HRPP (e.g., study coordinator), or, at the assistant or clerical levels, a desire to learn and be an active participant in the regulatory, ethical, and procedural aspects that support an HRPP.

Supervision: The IRB Assistant is supervised by the IRB Administrators who, in turn, are supervised by the Assistant Director of ORC. The Assistant Director of ORC reports to the AVP-RC.

Evaluation: Research Foundation and SUNY policy requires that a written evaluation and performance program be completed for its employees on an annual basis.

The program is designed to:

- Increase communication between an employee and his/her supervisor by setting forth clearly what the employees is expected to accomplish, what factors are important to successful performance, and at the end of the program period, how well the employee met his/her supervisor's expectations of job performance.
- Identify areas where additional training or development will improve performance.
- Assist an employee's supervisor in recognizing and rewarding his/her accomplishments.

When an individual is hired or is transferred to a new position the employee and his/her supervisor will meet to discuss the supervisor's performance expectations for the following year. During the year, a supervisor will discuss performance with each employee and provide feedback on progress as well as guidance for improvements as necessary.

At the end of the performance evaluation period, (typically the 12-month period following the establishment of the performance program), the supervisor will complete a Performance Evaluation Form for each employee. Each employee is encouraged to participate in the performance program and performance evaluation process by completing a self-appraisal, which is encouraged, but not required.

All HRPP employees are required to take and pass the Certification of IRB Professionals (CIP) examination within 3 years of hire.

1.12 Human Research Protection Program Resources

The ORC, is located within the Melville Library on Main Campus of the University and is equipped with all necessary office space, meeting space, storage space and equipment to perform the functions required for the HRPP.

The IO ensures procurement of adequate resources to the IRBs and ORC, including adequate meeting and office space, and staff for conducting IRB business. Office equipment and supplies, including technical support, file cabinets, computers, software, laptops, internet access, and copy machines, are made available to the IRBs and ORC staff.

The adequacy of personnel and non-personnel resources of the HRPP program, including the IRB committees and ORC is assessed on an annual basis by the AVP-RC, in consultation as required, with the Director of Grants Management, the Financial Administrator of ORC, and representatives from other administrative units, as applicable. The IO is advised of the outcome of this assessment for further action as required.

1.13 Conduct of Quality Assurance/ Quality Improvement Activities for the IRB Operation

The objective of the University's HRPP Quality Assurance / Quality Improvement Plan is to measure and improve human research protection effectiveness, quality, and compliance with organizational policies and procedures and applicable local, state, and local laws. The Quality Assurance/Quality Improvement Plan will be managed and implemented by the AVP-RC. Examples of types of goals and measures that might be adopted by the organization with respect to achieving and maintaining compliance include monthly measures of volume and efficiency. The goal would be to decrease the amount of time from study submission to approval for exempt, expedite, and full board research. Monthly, quarterly and annual metrics would be communicated to researchers/research staff (via the Office of Research Compliance website) as well as to HRPP staff and IRB chairs and members and administrators. One measure of effectiveness is the use of a satisfaction survey. Satisfaction surveys are sent to researchers and study conduct persons in order to evaluate the effectiveness of the program. Once a study has been approved the survey is sent. This allows the program to receive "real time" information regarding program effectiveness as experienced by the end users (e.g., researchers and research staff). The satisfaction survey includes a text section allowing the individual completing the survey to include information for improving the program or giving the program positive feedback.

1.13.1 Directed Audits

Directed audits of research studies approved by any SBU-recognized IRB are initiated in response to issue(s) identified by the IRB, the ORC, or complaint/concern filed by a subject, investigator, or

any party. Such audits will be conducted by the QA Administrator, but may include other ORC staff, IRB members and/or others as appropriate.

Depending on the specific issue being investigated**,** activities of auditors during directed audits may include examining investigator-held research records, patient medical records, financial disclosure forms, and other activities as deemed appropriate by IRBs.

1.13.2 Not-for-Cause Reviews

For every active study undergoing continuing review, a not-for-cause review is undertaken by the ORC staff as follows: Required with continuing review submissions are copies of the consent/permission/assent documents signed by the last subject enrolled. These documents have subject signature and name redacted, leaving intact all dates and the name of the person who obtained consent. For studies that are more than minimal risk, redacted copies of the inclusion/exclusion (I/E) checklist that was completed for that last enrolled subject is also required. Random audits of source documents that support the information on the completed I/E checklist is also performed. These documents are reviewed for correct version status, accurate completion, and identity of the person obtaining consent (is the individual an approved investigator on the study? Is human research training completed and current?). Any non-compliance uncovered as a result of this not-for-cause routine review is brought to the next scheduled IRB meeting for committee deliberation.

NOTE: SBU HRPP also has a formal consent monitoring program. See SOP section 3.9.4 'Consent Monitoring'

1.13.3 Non-University Institutional Audits

External directed ("for cause") audits will be done on activities conducted at non-University sites, where the IRB serve as the "IRB of Record," in response to concerns regarding compliance with federal, state, and local law, research subject safety, and IRB policies and procedures. These audits may include activities listed above.

1.13.4 Reporting and Disposition

Noncompliance revealed from directed audits and not-for-cause reviews will be reported to the AVP-RC, as well as to the applicable IRB at the next scheduled meeting. For issues concerning studies under external IRB oversight, reporting will occur at the next scheduled on-site IRB meeting. If the issue concerns an investigator, and is not study specific, all affected IRBs will be notified of findings). Any noncompliance will be handled according to the procedures in these SOPs.

If an audit or review finds potential serious or continuing noncompliance, and/or that subjects have been exposed to, or in danger of being exposed to conditions that compromise their safety, the IO, AVP-RC, and/or IRB Chair will be authorized to take immediate action as deemed necessary (prior to review or request for further investigation by the IRB), to ensure that the study subjects' health and welfare are protected.

Findings from audits are reviewed by the AVP-RC, ORC staff and applicable officials to determine if investigators might benefit from additional education or guidance (via e-mail) impacting the compliant and ethical conduct of their research activities, and whether study applications need to be clarified or revised to facilitate compliance.

1.13.5 IRB Internal Compliance Reviews

- The Office of Research Compliance staff conduct review of on-site IRB minutes and other meeting documents to determine that adequate documentation of the meeting discussion occurred and that appropriate actions and determinations have been made. This review includes assessment that , e.g., federal approval criteria have been considered and met (in approved studies, or met pending prescriptive revisions by the investigator), quorum is met and maintained, appropriate handling of COI management plans for investigators, appropriate recusal of conflicted members, appropriate committee action for substantive modifications, documented protocol-specific determinations for protections of vulnerable populations, and quality of IRB member reviews.
- The IRB staff ensures that, for continuing reviews, no lapse in approval has occurred and if it has, they will obtain a report from the PI detailing activities that transpired during the period of study lapse. Any activity that has transpired will be brought to the following IRB meeting for assessment of noncompliance. The staff will also verify other IRB approvals from (and Federal Wide Assurances where federal monies are involved) for collaborating institutions or external performance sites
- The AVP-RC and IRB staff routinely review HRPP standard operating procedures and other documents to ensure consistency with practice.
- Other monitoring or auditing activities will be conducted as deemed appropriate by the AVP-RC.

1.13.6 HRPP Quality Improvement

The AVP-RC, in consultation with the IRB Chairs and staff as deemed appropriate, defines (in an ongoing process) at least one targeted measure of operational efficiency and effectiveness and at least one targeted measure of compliance within the HRPP. In order to evaluate whether the defined goals are being achieved, data are reviewed and changes are instituted (e.g., education is

conducted, processes modified etc.) by the AVP-RC regularly. The IO and IRBs are informed of outcomes as applicable. Outcomes will often drive targeted educational opportunities to the campus community.

1.14 Multi-site Research

When engaged in non-exempt human subjects research (or exempt research for which limited IRB review is required) that is multi-site , involving external collaborators, or that is otherwise under the jurisdiction of more than one IRB, the University acknowledges that each organization is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable federal regulations. The University may choose to review the research in its entirety, only those components of the research the University is engaged in, rely on the review of another qualified IRB, or make other arrangements for avoiding duplication of effort. When the University is the prime awardee on a HHS grant, it will ensure that at least one IRB reviews the research in its entirety (see section 17.16 regarding the single IRB requirement for multicenter grants awarded from NIH, where all sites are conducting all research procedures).

When relying upon another IRB or when serving as the reviewing IRB for an outside organization or external investigator, a formal relationship must be established between the University and the outside organization or investigator through an IRB Authorization Agreement, a Memorandum of Understanding, or other such written agreement. The written agreement must be executed before the University will accept any human research proposals from the outside organization or investigator or rely on the review of an external IRB.

IRB reliance agreements establish the authorities, roles, and responsibilities of the reviewing IRB and the relying organization. The procedures for reliance, including for communication, information-sharing, and reports, may be outlined in the reliance agreement or in companion SOPs or other materials. The Reliance Administrator in the Office of Research Compliance utilizes a checklist to ensure that reliance agreements and any accompanying materials address all requirements and are consistent with the University's standards. To support compliance, the University will make every effort to ensure as much consistency as possible across reliance agreements.

The University has signed the SMART IRB joinder agreement. When the organizations participating in the research are signatories to the joinder agreement, IRB reliance may be requested and documented utilizing the SMART IRB online reliance platform. The University will determine on a study-by-study basis whether the SMART IRB SOPs or alternative procedures will be utilized to implement the reliance via a reliance arrangement agreed upon between the relying and reviewing sites.

Requests for SBU to either rely upon an external IRB or to serve as the IRB of record for an external organization or investigator should be submitted as early as possible in the grant/contract process by submitting a reliance request following the instructions in section 17.16 these SOPs.

See section 17.16 for procedures and considerations involved in IRB reliance arrangements.

If the SBU PI is the lead investigator, or the University is the coordinating center for multi-site or collaborative research, regardless of location of the research, the PI must document how the research plan and issues relevant to the protection of human subjects (e.g., IRB initial and continuing approvals, reports of unanticipated problems, study modifications, interim reports) will be communicated among participating sites and investigators.

To this end, SBU's electronic management system permits web-based protocol sharing and collaboration with participating sites of all aspects of the IRB initial, continuing, and post-approval reporting submission requirements. As part of pre-review, the ORC staff ensures that the PI or other responsible party from each collaborating site has access to the study within the electronic management system in order to keep abreast of study status and to ensure reporting capabilities.

2 Institutional Review Boards (IRB)

2.1 Policy

The University has one on-site Institutional Review Board (IRB) appointed by the IO. The IRB prospectively review and make decisions concerning all non-exempt human research conducted at its facilities or by its employees or agents, under the auspices of the University. The IRB is responsible for the protection of rights and welfare of human research subjects. It discharges this duty by complying with the requirements of the Common Rule, FDA regulations, other relevant federal regulations, state regulations, the FWA; and University policies. All non-exempt human subjects research conducted under the auspices of the University must be reviewed and approved by an authorized IRB prior to the initiation of the research.

The University also routinely utilizes the services of three off-site IRBs. They are:

- Advarra: the Advarra IRB is required to be used by University investigators who wish to conduct industry-initiated, industry-funded research activities.
- National Cancer Institute's Adult CIRB: for applicable cooperative oncology group protocols involving adult subjects.

National Cancer Institute's Pediatric CIRB: for applicable cooperative oncology group protocols involving minor subjects.

Although the University has authorized a number of IRBs to fulfill this function, all on-site IRBs follow the same policies and procedures. The following describes the authority, role and procedures of the on-site IRBs.

2.2 IRB Authority

Under University policy P202R "Research Involving Human Subjects", the IRB is authorized to:

- To approve, require modifications to secure approval, or disapprove human subjects research activities, including exempt research activities under 45 CFR 46.104 for which limited IRB review is a condition of exemption (under 45 CFR 46.104(d)(2)(iii) and (d)(3)(i)(C))
- To require that informed consent is obtained and documented in accordance with regulatory and policy requirements unless the criteria for the waiver or alteration of such requirements has been satisfied and approved by the IRB. The IRB may require that information, in addition to that specifically mentioned in the regulations, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects

Regarding continuing review:

- **For research subject to the Common Rule:** To conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year;
- **For research subject to other regulations (e.g., pre-2018 Common Rule, FDA, DoJ) or requirements (e.g., grant or contract terms):** To conduct continuing review of research at intervals appropriate to the degree of risk of the research, but not less than once per year;

- Suspend or terminate approval of research involving human subjects not being conducted in accordance with University's IRB requirements or that has been associated with unexpected serious harm to subjects;
- Observe, or have a third party observe, the consent process; and
- Observe, or have a third party observe, the conduct of the research.

Research that has been reviewed and approved by the IRB may be subject to review and disapproval by officials of the institution. However, those officials may NOT approve research if it has not been approved by the IRB. University officials may strengthen requirements and/or conditions, or add other modifications to secure University approval or approval by another University committee. Such University-driven (as opposed to IRB driven) conditions/modifications to a study previously approved by the IRB will require approval by the IRB. The IRB staff, in

consultation with the applicable IRB chair as needed, will determine whether the changes require full or expedited review.

2.3 Number of IRBs

There is currently one (1) on-site and three (3) off-site IRBs that may review research under the auspices of the University.

The AVP-RC, with consultation from the IRB staff and the Chairs of the IRBs as needed, will review the activity of the IRBs on at least an annual basis and make a determination as to the appropriate number of IRBs that are needed for the University. This determination will be based on the evaluation of the amount and type of research activities handled between the IRBs.

2.4 Roles and Responsibilities

2.4.1 IRB Chair

The University Institutional Official appoints the IRB Chairs. Any change in appointment, including reappointment or removal, requires written notification.

An IRB Chair should be a highly respected individual, from within the University, fully capable of managing the IRB, and the matters brought before it with fairness and impartiality. The task of making the IRB a respected part of the institutional community will be shared between the AVP-RC, and IRB Chairs. The IRB Chairs will be primarily responsible for ensuring that the IRB is perceived as fair, impartial and immune to pressure by the University's administration, the investigators whose protocols/studies are brought before it, and other professional and nonprofessional sources.

The IRB Chairs are responsible for conducting the meetings and delegates to the IRB Administrators and Assistant (all IRB members) the responsibility of being signatory for correspondence generated by the IRB.

The performance of the IRB Chairs will be reviewed and provided with feedback on an annual basis by the AVP-RC. If an IRB Chair is not acting in accordance with the IRB's mission, following these policies and procedures, has an undue number of absences, or not fulfilling the responsibilities of the IRB Chair, he/she will be removed.

2.4.2 Subcommittees of the IRB

The IRB Chair, or as delegated to the IRB Administrators, may designate one or more other subcommittees of the IRB to perform duties, as appropriate, to review and undertake other IRB functions, and to make recommendations to the IRB as appropriate. The IRB Chair, will appoint IRB members to serve on each IRB Subcommittee created under this Section. The number and composition of the IRB Subcommittee members shall depend on the authority delegated by the IRB Chair to such IRB Subcommittee (e.g., merely making recommendations versus decision-making authority). If the IRB Subcommittee has decision-making authority, then its members and composition must comply with the requirements specified in Section 2.6 of this document. Members of the IRB Subcommittee must be experienced in terms of seniority on the IRB, and must be matched as closely as possible with their field of expertise to the study assigned to the IRB Subcommittee.

2.5 Membership of the IRB

IRB members are selected based on appropriate diversity, including consideration of race, gender, cultural backgrounds, specific community concerns in addition to representation by multiple, diverse professions, knowledge and experience with vulnerable subjects, and inclusion of both scientific and non-scientific members. The structure and composition of the IRB must be appropriate to the amount and nature of the research that is reviewed. Every effort is made to have member representation that has an understanding of the areas of specialty that encompasses most of the research performed at the University.

When the IRB regularly reviews research that involves subjects vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons (e.g., IRB members, alternate members, or consultants) who are knowledgeable about and experienced with such subjects should be present during the review of the research. NOTE: Pregnant women are also considered a vulnerable population per FDA regulations.

The IRB must promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects; and possess the professional competence necessary to review specific research activities. IRB members are prohibited from owning equity in the organization.

Individuals from the Offices of Sponsored Programs, Grants Management, Proposal Development, or Intellectual Property Partnersmay not serve as members of the IRB or carry out day-to-day operations of the review process. Individuals from these offices may provide information to the IRB and attend IRB meetings as guests.

2.6 Composition of the IRB

1. The IRB will have at least five members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the University.
2. The IRB will be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.In addition to possessing the professional competence necessary to review specific research activities, the IRB will be able to ascertain the acceptability of proposed research in terms of the University policies and regulations, applicable law, and standards of professional conduct and practice. The IRB will therefore include persons knowledgeable in these areas.
3. The IRB will include members who are knowledgeable about and experienced working with subjects vulnerable to coercion or undue influence (e.g., children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons) that are regularly included in the research under its review. Note: For research subject to FDA, pregnant women remain as an example of vulnerable subjects.
4. Every nondiscriminatory effort will be made to ensure that the IRB does not consist entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender (FDA requirement). The IRB shall not consist entirely of members of one profession.
5. The IRB includes at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas.
6. The IRB includes at least one member who is not otherwise affiliated with the University and who is not part of the immediate family of a person who is affiliated with the University.
7. The IRB includes at least one member who represents the general perspective of subjects.
8. One member may satisfy more than one membership category.
9. IRB Staff of the ORC may be voting members of the IRB.

2.7 Appointment of Members to the IRB

The IRB Chairs, AVP-RC or staff of ORC, IRB membership, or IO can identify the need for a new or replacement member, or alternate member. A candidate may be nominated by any of these individuals, department chairs, or by other applicable officials within the University. The AVP-RC receives the nomination and consults with the IRB Chairs and ORC Staff to determine the appropriateness of the candidate, based on qualifications, reputation, and needs of the particular committee.

Where there are no nominees, appropriate department chairs, program directors, or other University officials will be contacted in writing for candidate nominees by the AVP-RC.

The final decision in selecting a new member, and appointment thereof, is made by the IO. Appointments are made for a renewable two-year period of service. Members may resign by written notification to the AVP-RC or IO. Members may be removed on a for-cause basis by those individuals as well.

On an annual basis, the IRB Chair, IRB Staff, and the AVP-RC (on behalf of the IO) review the membership and composition of the IRB to determine if they continue to meet regulatory and institutional requirements. Members are evaluated and receive their evaluations annually.

2.8 Alternate Members

The appointment and function of alternate members is the same as that for primary the IRB members, and the alternate's expertise and perspective are comparable to those of the primary member. The role of the alternate member is to serve as a voting member of IRB when the regular member is unavailable to attend a convened meeting. When an alternate member substitutes for a primary member, the alternate member will receive and review the same materials prior to the IRB meeting that the primary member received or would have received.

The IRB roster identifies the primary member(s) for whom each alternate member may substitute. The alternate member will not be counted as a voting member unless the primary member is absent. The IRB minutes will document when an alternate member replaces a primary member.

2.9 IRB Member Conflict of Interest

No regular member, alternate member, ex officio member, or consultant may participate in the review of any research project in which the individual has a conflict of interest (COI), except to provide information as requested. It is the responsibility of each IRB member to disclose any COI in a study submitted for review and to then recuse him/herself. At convened meetings, the IRB member recuses himself from the deliberations and vote by leaving the room. Any primary, secondary, or expedited reviewer with a COI must notify the IRB staff who will re-assign the protocol.

All voting, alternate, and ex officio members of the IRB complete a “IRB Member Human Research Conflict of Interest Assessment Form” when first appointed and annually thereafter. [See Section 14 “Conflicts of Interest in Research” for a detailed description of managing conflicts of interest.”]. IRB Staff are informed by the AVP-RC or designee if a member has a significant financial interest so that review assignments can be managed accordingly.

Conflict of interest applies to review by a convened IRB, review by the expedited procedure, review of unanticipated problems involving risks to participants or others, or review of non-compliance with regulations or laws or the requirements of the IRB.

Committee members and consultants may find themselves with any of the following COIs when reviewing research:

- Where the IRB member or consultant is involved in the design, conduct, and reporting of the research.
- Where an immediate family member of the IRB member or consultant is involved in the design, conduct, and reporting of the research.
- Where the IRB member holds significant financial interests (See Section 14 for a definition of significant financial interests) related to the research being reviewed.
- Any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a protocol

The IRB Chair will poll IRB members at each convened meeting to determine if a COI exists regarding any protocols to be considered during the meeting and reminds them that they should recuse themselves by leaving the room during the discussion and vote of the specific protocol. IRB members with a COI are excluded from being counted towards quorum. All recusals by IRB members with COI are recorded in the minutes.

If the COI status of a IRB member changes during the course of a study, the IRB member is required to complete an amended "IRB Member Human Research Conflict of Interest Assessment Form" and submit the completed document to the AVP-RC, who will, in turn advise the IRB Staff of the change.

2.10 Use of Consultants

When necessary, the IRB staff or the IRB members may solicit individuals from within or outside the University competence in special areas to assist in the review of issues or protocols, which require appropriate scientific or scholarly expertise beyond or in addition to that available on the IRB. The need for a consultant may be determined in advance of, or during the review of the study at, the meeting. The ORC staff ensures that all relevant materials are provided to the consultant in a timely manner following determination that an outside review is required. When the convened IRB requires consultation by individuals with appropriate expertise, the study will be tabled and reviewed at the next convened IRB meeting. Recommendations for consultants can be made by the IRB or the IRB staff.

Written statements of consultants will be kept in IRB records. Key information provided by consultants at meetings will be documented in the minutes. Written reviews provided by the outside reviewer will be filed with the study.

The AVP-RC reviews the COI policy for IRB members or consultants who must document for the record that they do not have a COI prior to review. Individuals who have a COI or whose spouse or dependent child have a COI with the sponsor of the research will not be invited to provide consultation.

The consultant's findings will be presented to the full board for consideration either in person or in writing. If in attendance, these individuals will provide consultation but may not participate in discussion or observe the vote.

Ad hoc or informal consultations requested by individual members (rather than the full board) will be requested in a manner that protects the investigator's confidentiality and is in compliance with the IRB conflict of interest policy (unless the question raised is generic enough to protect the identity of the particular PI and research protocol).

2.11 Duties of IRB Members

The agenda, submission materials, protocols, proposed informed consent forms and other appropriate documents are made available electronically to members approximately one week prior to the convened meeting at which the research is scheduled to be discussed. IRB members will treat the research proposals, protocols, and supporting data confidentially.

2.12 Attendance Requirements of the IRB Members

IRB members should attend all meetings for which they are scheduled. If an IRB member is unable to attend a scheduled meeting, they should inform an ORC staff member as soon as possible. If the inability to attend will be prolonged, a request for an alternate to be assigned may be submitted to the AVP-RC.

If an IRB member is to be absent for an extended period of time, such as for a sabbatical, he or she must notify the IRB at least 30 days in advance so that an appropriate replacement can be obtained. The replacement can be temporary, for the period of absence, or permanent, following consideration by the AVP-RC. If the IRB member has a designated alternate, the alternate can serve during the primary IRB member's absence.

2.13 Training/ Ongoing Education for the IRB Chair and Members

A vital component of a comprehensive human research protection program is an education program for IRB Chairs and IRB members. The University is committed to providing training and an on-going educational process for IRB members and ORC staff related to ethical concerns and regulatory and University requirements for the protection of human subjects.

Training

New IRB members, including alternate members, will meet with the AVP-RC or designee for a formal orientation/training session. At the session, the new IRB member will be given:

- Web links to the SBU Human Research Protection Program and SOPs
- Belmont Report;
- Stony Brook University HRPP Standard Operating Procedures;
- Federal regulations relevant to IRB.
- Reviewer worksheets and checklists
- Copy of the IRB Member Module ("What Every New IRB Member Needs to Know")

In addition to the training session, the IRB members will complete the Biomedical Basic CITI Training

Continuing Education

To ensure that oversight of human research is ethically grounded and the decisions made by the IRB is consistent with current regulatory and policy requirements, training is continuous for IRB members throughout their service on the IRB and monitored annually by the Office of Research Compliance staff to ensure compliance. If IRB members and IRB Chairs refuse to complete training requirements they are removed from the committee. Educational activities include, but are not limited to:

- In-service training at IRB meetings;
- Webinars;
- Copies of appropriate publications and articles;
- Identification and dissemination by the AVP-RC of new information that might have an effect on the human research protection program, including laws, regulations, policies, procedures,

and emerging ethical and scientific issues to IRB members via email, mail, or during IRB meetings.

IRB Chairs receive a monthly training during the IRB Chair meeting on a variety of topics pertinent to human subject protection.

The IO will provide support to send as many members of the IRB as are interested in attending the annual PRIM&R conference.

The IRB staff is required to complete applicable modules of the CITI Course in the Protection of Human Research Subjects. IRB staff will be expected to attend at least one conference/webinar (e.g., PRIMR, etc.) annually.

2.14 Liability Coverage for IRB Members

The on-site IRB is constituted by the State University of New York (SUNY). NYS Public Officers Law, section 17 provides that where the requirements of Public Officers Law section 17 are met, and contingent on a determination by the Attorney General of the State of New York, the state shall provide for the defense of state employees and officers in civil action or proceeding in any state or Federal court arising out of the any alleged act or omission which occurred or is said to have occurred while the state employee, or officer was acting within the scope of his/her public employment or duties carried out on behalf of the state.

2.15 Review of IRB Member Performance

Annually, the following will be conducted:

- The Chairs provide feedback on the members of their committee.
- The IRB Staff can provide feedback on the IRB members and Chairs.

The IO or designee takes the information above, along with attendance data, and writes an evaluation for each member and chair which is shared with them. The correspondence will either thank them for their continued service, or serve as notice that their services will not be necessary moving forward.

IRB members who are not acting in accordance with the University mission or its policies and procedures may be removed outside of the formal annual evaluation process.

The IRB members who are also IRB staff are annually evaluated by the AVP-RC.

2.16 Reporting and Investigation of Allegations of Undue Influence

If an IRB Chair, member, or staff person feels unduly influenced by any party, they are to make a confidential report to the IO or AVP-RC, depending on the circumstances. The official receiving the report will conduct a thorough investigation and corrective action will be taken to prevent additional occurrences.

3 IRB Review Process

3.1 Policy

All human subjects research conducted under the auspices of the University must meet the criteria for one of the following methods for review:

- Exempt
- Expedited Review
- Full Committee Review

The IRB will ensure that the research meets all required ethical and regulatory criteria for initial and continuing review and any modifications of approved research.

The following describe the procedures required for the review of research by the IRB.

3.2 Definitions

Minimal Risk: the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For Department of Defense research, minimal risk based on the phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests" shall not be interpreted to include the inherent risks certain categories of human participants face in their everyday life. For example, the risks imposed in research involving human participants focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain.)

Minor Change: a change, in the judgment of the IRB reviewer, which makes no substantial alteration in:

- Level of risks to subjects

- Research design or methodology (adding procedures that are not eligible for expedited review would not be considered a minor change)
- Number of subjects enrolled in the research
- Qualifications of the research team
- Facilities available to support safe conduct of the research
- Any other factor which would warrant review of the proposed changes by the convened IRB

Quorum: consists of a simple majority of the voting membership, including at least one member whose primary concern is in a non-scientific area. If research involving an FDA-regulated article is involved, a licensed physician must be included in the quorum.

Suspension of IRB approval: a directive of the convened IRB or other authorized individual to temporarily stop some or all previously approved research activities short. Suspended protocols remain open and require continuing review.

Termination of IRB approval: a directive of the convened IRB to stop permanently all activities in a previously approved research protocol. Terminated protocols are considered closed and no longer require continuing review.

3.3 Electronic Management System

The University uses an electronic management system for administration and management of its IRBs. This system provides electronic management of protocols and documents; on-line submissions; web-based protocol sharing and collaboration; automatic notifications; the furnishing of electronic signatures; event tracking; and other important electronic features. The system tracks all open studies, even if ongoing review by an IRB is not required. The University began requiring electronic protocol submissions effective December 2007. All protocols, including revisions and renewals, must be submitted electronically via the electronic management system, and all review decision notifications are issued electronically via the electronic management system. Instructions for the use of this system are located on the ORC website.

3.4 Human Subjects Research Determination

Some University activities involve people (e.g., academic classroom activities, hospital quality assurance/quality improvement [QA/QI] etc.) but that does not mean that it falls under the category of human subject research.

The responsibility for initial determination as to whether an activity constitutes human subjects research rests with the investigator. The investigator should make this determination based on

the definitions of “human subject” and “research”. Since the University will hold them responsible if the determination is not correct, investigators are urged to request a confirmation that an activity does not constitute human subjects research from the ORC. The request should be made with the electronic management system. All requests must include sufficient documentation of the activity to support the determination.

NOTE: With the implementation of the revised Common Rule, the requirement of the Newborn Screening Saves Lives Reauthorization Act of 2014 that federally-funded "research on newborn dried blood spots shall be considered research carried out on human subjects" is eliminated. Whether such research involves human subjects shall now be considered using the same standards as are used for other research involving human biospecimens (e.g., whether the identity of subjects may be readily ascertained, whether the specimens are coded and who has access to the key, whether the research involves the evaluation of the safety or effectiveness of an FDA-regulated device, etc.).

In response to investigator requests, determinations that an activity does not constitute human subjects research will be documented using the **Human Subjects Research Determination form**. For activities determined to constitute human subjects research, the investigator will be notified by the the HRPP and instructed to begin with the exemption or IRB application process, as applicable.

NOTE: *The University has a policy regarding the distinction between QA/QI initiatives and research activities. The section on* ***“Quality Assurance/Quality Improvement (QA/QI) Activities vs. Research Activities”*** *should be reviewed for details.*

3.4.1 Case studies/Series

A case study/series is an analysis of up to 3 clinical cases and usually examines a condition, treatment, presentation, or outcome. If the analysis involves more than 3 cases it would need to be reviewed by the Human Research Protection Program and an application would need to be completed in the electronic management system myResearch.

A case study/series is not meant to draw broad conclusions about a population and does not meet the DHHS definition of research which is “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.”

Although the use of Protected Health Information for a case study/series does not require IRB review, the Health Insurance Portability and Accountability Act (HIPAA) requires written authorization for certain uses and disclosures of a patient’s Protected Health Information. This

requires that the patient sign an Authorization Agreement. Or, the parent or legally authorized representative (if the patient is deceased or lacks capacity to consent) must sign for the use of the patient's information in the article. Otherwise, the Stony Brook University IRB Chair or IRB would need to waive the requirement for HIPAA Authorization.

An Authorization Agreement may not be required if the patient information is not identifiable. This would include that no photographs of the patient be disclosed and that there not be any identifiable patient features (i.e., tattoos, unusual scar or birthmark). Additionally, the information in the case study should not be so unique as to be identifiable to the patient's family or others known to the patient.

NOTE: Some journals now require a letter or other form of acknowledgement from the Institutional Review Board prior to the submission of a case study/series to a journal. Please click on the memo on the website at https://www.stonybrook.edu/commcms/research-compliance/Human-Subjects/sops. This memo may then be sent to the journal confirming the Stony Brook University policy.

3.5 Exempt Studies

All research using human subjects must be approved by SBU. Although certain categories of human subject research are exempt from IRB oversight, the determination of exempt status at SBU must be made by ORC Staff. These individuals are not involved in the proposed research and must not have any apparent conflict of interest. Reviewers will use the **Reviewer Exemption Determination Checklist** to determine and document whether the protocol meets the exemption criteria.

SBU may also choose to accept an exempt determination made by an external IRB; SBU will consider such requests on a case by case basis.

Unless otherwise required by law or by Federal department or agency heads, exempt studies are exempt from the requirements of the Common Rule (i.e., IRB approval and full research consent are not required) other than as specified within the regulations (e.g., the conditions that permit exemption, and when limited IRB review is required). Exempt research (including limited review) is not exempt from ethical considerations, such as honoring the principles described in the Belmont Report. The individual/s making the determination of exemption will determine whether to require additional protections for subjects in keeping with ethical principles (e.g., requiring disclosure/consent, etc.).

The exemption is valid for the life of the project or when the project changes in any way (therefore requiring amendment) whichever comes first. Investigators must communicate to ORC any changes proposed during the conduct of the activity so that it may be reviewed to determine if the exemption still applies. Decisions regarding exemption determination will be provided in writing to the investigator. Documentation will include the specific category/categories justifying the exemption. Consent obtained for an exempt research study will contain the following information:

- The activity involves research
- Description of the procedures
- Participation is voluntary
- Name and contact information for the researcher
- Adequate provisions are in place to maintain the privacy interests of the participants

3.5.1 Limitations on Research Subjects:

Vulnerable Populations:

Children: Exemption #2(i) and (ii) for research involving survey or interview procedures or observations of public behavior does NOT apply to research in children, except for research involving observations of public behavior when the investigator does not participate in the activities being observed. Exemption #2(iii), where identifiable information is obtained and the IRB conducts a limited IRB review, is NOT applicable to research with children. Exemption #3 does NOT apply to research involving children. [45 CFR 46.104(b)(3)]

Prisoners: Exemptions do not apply except for research aimed at involving a broader subject population that only incidentally includes prisoners. [45 CFR 46.104(b)(2)]

3.5.2 Categories of Exempt Research

With the above exceptions and any other limitations or restrictions due to applicable law, regulation, or agency policy, research activities not regulated by the FDA (see Section 3.5.3 for FDA Exemptions), in which the only involvement of human subjects are determined to be in on or more of the following categories may be determined to be exempt:

Note:

- *See also Special Topics Section **(Data/Tissue Registries/Banks)** and **(Guidance on Research (only) Involving Coded Private Information or Biological Specimens)** for information that may be relevant to the activity in question.*

- *SBU at this time has **not** adopted Broad Consent and therefore cannot accept applications for exempt categories reviewed under 45 CFR 46.104 (d)(7) and (8).*
    1. Research, conducted in established or commonly accepted educational settings, *which* specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

    2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

        i. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
        ii. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
        iii. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7): *When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data*.

    3. (i) Research involving benign behavioral interventions (See additional information below) in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

        A. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
        B. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

C. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7): *When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data*.

(ii) For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

(iii) If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

   i. The identifiable private information or identifiable biospecimens are publicly available;
   ii. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;
   iii. The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b); or
   iv. The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for

nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

NOTE: This exemption permits the secondary research use of identifiable private information or identifiable biospecimens obtained from subjects who are prisoners, if the research is not designed in a way that seeks to recruit prisoners as a population but rather only incidentally (i.e., not intentionally) includes prisoners)

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.
    i. Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal website or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

6. Taste and food quality evaluation and consumer acceptance studies:

    i. If wholesome foods without additives are consumed, or
    ii. If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by

the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

3.5.3 Food and Drug Administration (FDA) Exemptions

The following categories of clinical investigations are exempt from the requirements of prior IRB review:

- Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the University is subject to IRB review. [21 CFR 56.104(c)]

Note: *See section 7.2* ***(FDA Exemptions)*** *for a detailed discussion of this exemption.*

- Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or approved by the EPA or the FSIS of the USDA. [21 CFR 56.104(d)]

3.5.4 Additional Protections

Although exempt research is not covered by the federal regulations, this research is not exempt from the ethical guidelines of the Belmont Report. The individual making the determination of exemption will determine whether to require additional protections, including a requirement for informed consent.

3.5.5 Materials to be Submitted for IRB Review of Exemption Request

The following materials will be completed/submitted via the electronic management system:

- Exempt Application
- Study Protocol
- Informed consent documents, as applicable
- HIPAA relevant forms (see Section 16)
- Recruitment materials/subject information
- Data collection instruments (including all surveys and questionnaires)
- Supplemental forms as applicable (e.g., international research, minors etc.)
- University Hospital Approval form (if applicable)

The application package must be electronically signed and dated by the responsible principal investigator and the departmental/departmental review committee chair in order for the application to be reviewed. If the activity will impact another department (e.g., use of their resources, i.e., facilities, patient populations, faculty, and/or staff, etc.), electronic signature of that department's chair is required as well. Grant applications will not be reviewed by the Office of Research Compliance.

The primary reviewer for the submission will be one or more IRB Administrators/Assistants within the ORC. Investigators will receive feedback via the electronic management system regarding the results of review. Possible determinations include Approved (for exemption status), Modifications required (in order to secure exemption status), or Not Approved (letter from the ORC would either clarify that the study is not acceptable to conduct at the University, or the study does not qualify for exempt status, i.e., activity requires either expedited or full committee review).

When the research requires limited IRB review or a HIPAA determination (i.e., waivers or alterations of the requirement for HIPAA authorization), the review may be conducted using expedited review procedures by the IRB Chair or an experienced Chair-designated member of the IRB. As with all other research subject to IRB review requirements, when conducting limited IRB review the IRB has the authority to approve, require modifications in (to secure approval), or disapprove all research activities; and to suspend or terminate IRB approval. Actions of disapproval may only be made by the convened IRB. [45 CFR 46.109(a), 45 CFR 46.110]

Proposed modifications to the aspects of research subject to limited IRB review must be submitted to and approved by the IRB prior to implementation, except when necessary to eliminate apparent immediate hazards to the subject(s), in which case the change must be promptly reported to the IRB (i.e., within 10 business days). [45 CFR 46.108(a)(3)(iii)]

Continuing review is generally not required for research determined to be exempt, even when that research is subject to limited IRB review. However, the IRB may determine that continuing review is required for a particular study subject to limited IRB review, in which case the reviewer will document the reasons for its determination in the IRB record and communicate the requirement to the investigator in the IRB determination letter. [45 CFR 46.109(f)(ii), 45 CFR 46.115(a)(3)]

3.6 Expedited Review

The IRB may use the expedited review procedure to review either the following:

1. Some or all of the research appearing on the list of categories of research eligible for expedited review, **unless** the reviewer determines that the research involves more than minimal risk. (For

research subject to FDA, the reviewer must also determine that the research involves no more than minimal risk.)
2. Minor changes (as defined in section 3.2) in research previously approved by the convened IRB. Note: review of minor changes does not alter the end-date of study approval.
3. Research for which limited IRB review is a condition of exemption under 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(c) as well as (d).

3.6.1 Categories of Research Eligible for Expedited Review

- For activities subject to the Common Rule, if an activity is covered by one or more of the categories below, it is presumed to be minimal risk, **unless the reviewer determines and documents that the study involves more than minimal risk.**
- For activities subject to FDA regulation, the activities listed below should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects. The reviewer must specifically determine that the activity is minimal risk.

The categories in this list apply regardless of the age of subjects, except as noted in category 2 below.

The expedited review procedure **may not** be used:

- Where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
- For classified research involving human subjects.

Research Categories one (1) through seven (7) pertain to both initial and continuing IRB review:

Note: See also Special Topics Section 17.2 ***(Data/Tissue Registries/Banks)*** *and 17.5 (****Guidance on Research (only) Involving Coded Private Information or Biological Specimens)*** *for information that may be relevant to the activity in question.*

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met:
   a. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or

decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)

b. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
   a. From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an eight (8) week period and collection may not occur more frequently than two (2) times per week; or
   b. From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an eight (8) week period and collection may not occur more frequently than two (2) times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means.

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

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications).

Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

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

   Note: *Some research in this category may be exempt from the DHHS regulations for the protection of human subjects.* See Exempt Categories and 45 CFR 46 101(b)(4). This listing refers only to research that is not exempt.

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

   Note: *Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. See Exempt Categories and 45 CFR 46.101(b)(2). This listing refers only to research that is not exempt.*

   Categories 8 and 9 only apply to continuing review.

8. Continuing review of research previously approved by the convened IRB as follows:

   a. Where:
      i) the research is permanently closed to the enrollment of new subjects;
      ii) all subjects have completed all research-related interventions; **and**
      iii) the research remains active only for long-term follow-up of subjects (Note: "Long-term follow-up" includes research *interactions* that involve no more than minimal risk to subjects (e.g., quality of life surveys); and collectio*n of follow-u*p data from procedures

or interventions that would have been done as part of routine clinical practice to monitor a subject for disease progression or recurrence, regardless of whether the procedures or interventions are described in the research study, but not *interventions* that would **not** have been performed for clinical purposes, even if the research interventions involve no more than minimal risk.);

Or

b. Where no subjects have been enrolled at SBU and no additional risks have been identified (Note: “no additional risks have been identified” means that neither the investigator nor the IRB has identified any additional risks from any institution engaged in the research project or from any other relevant source since the IRB’s most recent prior review);

Or

c. Where the remaining research activities at SBU are limited to data analysis

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

   Under Category (9), an expedited review procedure may be used for continuing review of research not conducted under an investigational new drug application or investigational device exemption where categories (2) through (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified. The determination that "no additional risks have been identified" does not need to be made by the convened the IRB.

3.6.2 Materials to be Submitted for IRB Expedited Review

The following summarizes the document requirements for submission to the IRB:

For initial submissions:
Registration Form and /or* Application
Study protocol
Consent/permission/assent documents
Recruitment materials
Data collection sheets (e.g., spreadsheets, case report forms)

Surveys, questionnaires
As applicable:

Supplemental Forms:

- A: Pregnant Women, Fetuses, Non and Questionably Viable Neonates
- B: Prisoners
- C: International Research
- D: ICH-GCP
- E: Minors
- G: Consent Waivers

HIPAA forms
University Hospital Approval form
Protocol Review Committee (PRC) Approval (oncology studies only)
Fee authorization form (for industry studies going to CRRI)
Scientific merit review (for industry studies going to CRRI or NCI CIRB)
Inclusion/exclusion checklist (if requested by IRB reviewer)

For continuing review submissions (If continuing review applies):
Registration Form and /or Application
Study protocol
Recruitment materials
Redacted consent/permission/assent documents of last subject enrolled
As applicable:

- Data safety monitoring board reports
- Gov't or sponsor audit/monitoring reports
- Clean, current inclusion/exclusion checklist (if requested by IRB reviewer)
- Redacted I/E checklist of last subject enrolled (If study was approved with one)

Prior to access of materials by the IRB members, IRB staff will verify that the application is electronically signed by the responsible principal investigator and the departmental/departmental review committee chair; If the activity will impact another department (through use of their resources, e.g., facilities, patient populations, faculty, and/or staff, etc.) e-signature of that department's chair will be required as well.

The determination of which committee receives an initial study for expedited review is made by the IRB staff on an alternating basis.

3.6.3 Expedited Review Procedures

Under an expedited review procedure, IRB review is carried out by the IRB Chair or by one or more reviewers designated by the Chair from among experienced members and alternate members of the IRB. Designated reviewers must be professionally competent (i.e., experienced with and having demonstrated the ability to apply IRB review requirements and with appropriate scientific or scholarly expertise) to conduct expedited reviews.

When reviewing research under an expedited review procedure, the designated IRB member(s), will have access to all submitted documentation, as well as pre-review comments from the IRB staff, and, in the case of a continuing review, all study history, which resides in the electronic management system.

In reviewing initial, or continuing research, the reviewers will follow the Review Procedures described in Sections 3.8 and 3.9 and may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may only be disapproved by the IRB following review at a convened meeting.

Reviewers will use the IRB Reviewer Checklist as an aid to complete the IRB Member Worksheet(s) for Expedited Reviews, including assessment that the regulatory criteria necessary for expedited review and IRB approval have all been met, and indicate approval, required modifications or 'deferred to full committee'. The Worksheet will be retained within the electronic management system to ensure documentation of regulatory determinations. The IRB Administrators/Assistant will draft an applicable letter and post it, along with associated documents (e.g., track-changed consent forms, etc.), within the electronic management system.

When a reviewer determines that research subject to the Common Rule falls within the expedited categories but involves more than minimal risk, the reviewer will document the rationale for that determination in the checklist and refer the research for review by the convened IRB.

Investigators are notified by the electronic management system when an action is taken on a study. If the modifications are prescriptive, the IRB staff, as IRB members, may serve as final reviewers to determine if the investigator has satisfied the conditions for approval. If the modifications are substantive, if the reviewer(s) request it, or if the IRB staff deem it necessary, the modified submission will be sent back to the IRB member(s) for further review. If the reviewer determines that the research does not meet the criteria for expedited review (or for any other reason), then the reviewer will indicate that the research requires full review by the IRB and the study will be placed by the IRB Staff on the next available agenda for an IRB meeting.

3.6.4 Informing the IRB

All members of the IRB will be apprised of all expedited review approvals, including limited IRB reviews conducted using expedited review procedures by means of a list in the agenda for the next scheduled meeting. Any IRB member can request to review the full protocol by contacting the ORC.

3.7 Convened IRB Meetings

Except when an expedited review procedure is used (including exempt research subject to limited IRB review), the IRB will conduct initial and continuing reviews of all non-exempt research at convened meetings at which a quorum (see below) of the members is present.

3.7.1 IRB Meeting Schedule

The IRB meets weekly throughout the year. The meeting schedule for the IRBs may vary due to holidays or lack of quorum. The schedule of meeting deadlines and meeting dates is available on the ORC website.

Special meeting can be called at any time by the IRB Chair, the AVP-RC, or the IO.

3.7.2 Preliminary Review

ORC staff will perform a preliminary review of all study materials submitted for IRB review for determination of completeness, accuracy, special regulatory considerations, and required electronic signatures (department chair, principal investigator). Only complete submissions will be placed on an IRB agenda for review. The investigator will be notified of missing information through the electronic management system.

3.7.3 Primary and Secondary Reviewers

After it has been determined that the research study submission is complete, the IRB Staff will assign the research study to reviewers paying close attention to the scientific content of the protocol, the potential reviewer's area of expertise, and ensuring, where applicable, that a scientific and non-scientific perspective is represented. Two reviewers will be assigned to each initial or continuing protocol and a reviewer may be assigned several protocols or other research items for review (generally, one reviewer is assigned to a protocol brought to committee for a modification/amendment review). When the IRB is presented with a protocol that may be outside of the knowledge base of any of the IRB members, an outside consultant will be sought.

Protocols for which appropriate expertise cannot be obtained for a given meeting will be tabled and moved to a subsequent meeting agenda.

The primary and secondary reviewers are responsible for:

1. Having a thorough knowledge of all of the details of the proposed research.
2. Performing an in-depth review of the proposed research.
3. Leading the discussion of the proposed research at the convened meeting, presenting both positive and negative aspects of the research, and leading the IRB through the regulatory criteria for approval.
4. Making suggestions for changes to the proposed research, where applicable.
5. Completing all applicable IRB reviewer forms.

If both the primary and secondary reviewer are absent from the meeting, consensus shall be taken to determine if the study in question will be tabled for a review at a future meeting, or if the present members have sufficient information and expertise, then review will proceed. Additionally, an absent reviewer can submit their written comments for presentation at the convened meeting, as long as there is another reviewer present at the convened meeting, who can serve as the primary reviewer. It should be noted that all of the IRB members receive and are expected to review all studies, not just the ones they for which they are assigned as primary or secondary reviewer.

3.7.4 Pre-Meeting Distribution of Documents

The study, including all required materials, needs to be submitted by the deadline for a particular meeting for inclusion on the applicable IRB agenda. The meeting agenda will be prepared by the IRB Staff and made available to the IRB members via the electronic management system prior to the meeting. All IRB members receive access to meeting protocol review materials, no later than five (5) business days before the scheduled meeting to allow sufficient time for the review process. Prior month's meeting minutes, applicable business items and audits, and appropriate continuing education materials will be made available to the members as far ahead of the meeting as possible.

3.7.4.1 Investigator Contact Before the Meeting

To improve efficiencies and communication between the IRB and investigators, and to supplement the IRB's review, the IRB members are strongly encouraged to contact PIs with questions and clarifications ahead of the meeting in order to facilitate the review process, and decrease the probability of a deferral or disapproval determination.

3.7.5 Materials to be Submitted for IRB Full Committee Review

Each IRB member will be given access to all submission materials for all studies on the agenda:

The following checklists summarize the document requirements for submission to the IRB:

For initial submissions:

Registration Form and /or Application
Study protocol
Consent/permission/assent documents
Recruitment materials
Data collection sheets (e.g., spreadsheets, case report forms)
Surveys, questionnaires
As applicable:

Supplemental Forms:

- A: Pregnant Women, Fetuses, Non and Questionably Viable Neonates
- B: Prisoners
- C: International Research
- D: ICH-GCP
- E: Minors
- G: Consent Waivers

HIPAA forms
University Hospital Approval form
Protocol Review Committee (PRC) Approval (oncology studies only)
Fee authorization form (for industry studies going to CRRI)
Scientific merit review (for industry studies going to CRRI or NCI CIRB)
Inclusion/exclusion checklist
Package inserts for approved drugs/devices
Investigator brochures for investigational drugs/devices

For continuing review submissions:

Registration Form and /or Application
Study protocol
Recruitment materials
Redacted consent/permission/assent documents of last subject enrolled

- Inclusion/exclusion checklist (clean, current)
- Redacted I/E checklist of last subject enrolled

As applicable:

- Data safety monitoring board reports
- Gov't or sponsor audit/monitoring reports

  The status report on the progress of the research includes:
  - The number of participants accrued.
  - A summary since the last IRB review of:
    - Adverse events and adverse outcomes experienced by participants.
    - Unanticipated problems involving risks to participants or others.
    - Participant withdrawals.
    - The reasons for withdrawals.
    - Complaints about the research.
    - Amendments or modifications.
    - Any relevant recent literature.
    - Any interim findings.
  - Any relevant multi-center trial reports.
  - The researcher's current risk-potential benefit assessment based on study results.

Prior to sharing submission materials with the IRB members, IRB staff will verify that the application package is electronically signed by the responsible principal investigator, and the departmental/departmental review committee chair. If the activity will impact another department's resources (e.g., use of their facilities, patient populations, faculty, and/or staff, etc.), electronic signature of that department's chair will be required as well.

Although the electronic management system permits all IRB members to review all materials submitted for review, the primary and secondary reviewers must review: any relevant grant applications; the sponsor's protocol (when one exists); the investigator's brochure (when one exists); the DHHS-approved sample informed consent document (when one exists); the complete DHHS-approved protocol (when one exists).

Reviewers will complete the IRB Member Worksheet(s) for Full Committee Review.

3.7.6 Quorum

A quorum consists of a simple majority (more than half) of the voting membership, including at least one member whose primary concern is in a non-scientific area. If the non-scientific member leaves the room, quorum is lost, and votes cannot be taken until the quorum is restored, even if half of the members are still present. If research involving an FDA-regulated article is involved, a licensed physician must be included in the quorum. The IRB Chair, with the assistance of the IRB

staff, will confirm that an appropriate quorum is present before calling the meeting to order. The IRB staff will be responsible for ensuring that the meetings remain appropriately convened.

A quorum must be maintained for each vote to occur. The IRB staff takes note of arrivals and departures of all members and notifies the chair if a quorum is not present. If a quorum is not maintained for reasons relating to an IRB member's recusal due to a Conflict of Interest, the individual proposal must be tabled. If quorum is lost for the remaining duration of the meeting, the meeting must therefore be terminated.

IRB members are considered present if participating through teleconference or videoconference. In this case, the IRB member must have received all pertinent material prior to the meeting and must be able to participate actively and equally in all discussions.

Opinions of absent IRB members that are transmitted by mail, telephone, facsimile, or e-mail may be considered by the attending IRB members but may not be counted as votes or to satisfy the quorum for convened meetings.

It is generally expected that at least one unaffiliated member and at least one member who represents the general perspective of subjects (the same individual can serve in both capacities) will be present at all IRB meetings. Although the IRB may (on occasion) meet without this representation, a best effort will be made to make sure that individuals serving in this capacity will be present for at least 80% of the IRB meetings.

3.7.7 Meeting Procedures

The IRB Chair, or designee in the event that the IRB Chair is absent, will call the meeting to order, once it has been determined that a quorum is in place.

The IRB reviews all submissions for initial and continuing review, as well as requests for modifications. The primary and secondary reviewers present an overview of the research and lead the IRB through the completion of the regulatory criteria for approval in the IRB Approval Criteria Worksheet, and other determinations that must be found and documented. When a study is funded by the Department of Defense, the ORC staff will review with the members the required information contained within the 'Meeting Final Determination: SUPPLEMENT: DODI, and complete the document to confirm compliance with Department of Defense Instruction 3216.02.

All members present at a convened meeting have full voting rights, except in the case of a Conflict of Interest. Where an IRB member and his/her alternate are both present, only the IRB member has voting rights. In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting.

It is the responsibility of the ORC staff to record final meeting determinations for each reviewed study at the meeting. This is accomplished via the minutes, the voting form and Final Meeting Determination forms that are on file in support of the minutes. For IRB meetings, members have access to laptops but may also use their own laptop in order to access the myResearch IRB electronic submission system. During the meeting, information is shared on a screen so that all members have access to all materials.

3.7.8 Guests

At the discretion of the IRB, the principal investigator may be invited to the IRB meeting to answer questions about their proposed or ongoing research. The principal investigator and/or members of the study team may not be present for the discussion or vote on their research.

Ex-officio guests are individuals who, by virtue of their position and their role in the HRPP, regularly attend IRB meetings. Examples of ex-officio guests include IRB staff who are not IRB members, the AVP-RC, and the IO. Ex-officio guests may fully participate in the IRB discussion and deliberations, but may not vote Individuals who are responsible for business development are prohibited from serving as mmnbers or ex-officio members on the IRB or carrying out day-to-day operations of the review process.

Other guests may be permitted to observe IRB meetings at the discretion of the IRB Chair, AVP-RC, or the IO.

3.8 Criteria for IRB Approval of Research

In order for the IRB to approve human subject research, it must determine that the following requirements are satisfied:

1. Risks to subjects are minimized: (i) by using procedures, which are consistent with sound research design and which, do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

3. Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving subjects vulnerable to coercion or undue influence, such as children, prisoners, mentally disable persons, or economically or educationally disadvantaged persons.
4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.117.
5. Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117.
6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
8. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

3.8.1 Risk/Benefit Assessment

The goal of the assessment is to ensure that the risks to research subjects posed by participation in the research are justified by the anticipated benefits to the subjects or society. Toward that end, the IRB must:

1. Where the risk is deemed more than minimal, judge whether the anticipated benefit, either of new knowledge or of improved health for the research subjects, justifies asking any person to undertake the risks,
2. Not approve research in which the risks are judged unreasonable in relation to the anticipated benefits.

The assessment of the risks and benefits of proposed research - one of the major responsibilities of the IRB - involves a series of steps:

1. Identify the procedures being conducted specifically for research;
2. Identify the risks associated with the research procedures, as distinguished from the risks of therapies the subjects would receive even if not participating in research;
3. Determine whether the risks will be minimized to the extent possible;
4. Identify the probable benefits to be derived from the research;

5. Determine whether the risks are reasonable in relation to the benefits to subjects, if any, and assess the importance of the knowledge to be gained;
6. Ensure that potential subjects will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits.

Risks to subjects are minimized:

1. By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk; and
2. Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

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

In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research.

The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

3.8.1.1 Scientific Merit

In order to assess the risks and benefits of the proposed research, the IRB must determine that:

- 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; and
- The knowledge expected to result from this research is sufficiently important to justify the risk.

In making this determination, the IRB draws upon (a) its own knowledge and disciplinary expertise, and (b) the knowledge and disciplinary expertise of others, such as departmental level review by chair or review committee (via e-signature on the submission to the IRB), and/or the peer review process of funding agencies.

Prior to the IRB review of new and continuing protocol applications, as well as major amendments, institutional scientific review is documented by the e-signature of the administrative official responsible for the investigator's research unit.

3.8.2 Selection of Subjects is Equitable.

The IRB determines by reviewing the application, protocol and other submission materials that the selection of subjects is equitable with respect to gender, age, class, etc. The IRB will not approve a study that does not provide adequately for the equitable selection of subjects or has not provided an appropriate scientific and ethical justification for excluding classes of persons who might benefit from the research.

In making this determination, the IRB evaluates: the purposes of the research; the setting in which the research occurs; scientific and ethical justification for including subjects vulnerable to coercion or undue influence such as such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons; the scientific and ethical justification for excluding classes of persons who might benefit from the research; and the inclusion/exclusion criteria.

At the time of the continuing review, the IRB will determine that the PI has followed the subject selection criteria that he/she originally set forth at the time of the initial the IRB review and approval.

3.8.2.1 Recruitment of Subjects

A study's recruitment plan and all study recruitment materials must be reviewed and approved by the IRB prior to use. The recruitment plan submitted to the IRB should be detailed with respect to media to be used (e.g. flyer, newspaper, video, radio etc.), location (e.g., specific sites named, on or off campus) and process (i.e., under what conditions will subjects be approached? etc.). When drafting the plan, the investigator must be aware of special approvals that may be required at sites she/he wishes to include in the recruitment plan. These approvals should be submitted for the IRB file.

It is the policy of the HRPP that when recruiting patients as potential subjects, first contact must be made by someone who has a relationship (e.g., treatment etc.) with the patient: When patients come to our hospital, they come for clinical reasons. It is therefore respectful to them to ensure that when they are initially approached about research, it is by someone who 'makes sense' to be approaching them, i.e., someone who has some type of relationship with them from their 'clinical world'. This policy protects the patient's right to privacy. See SOPs section 16.4.2. for a recruitment method that is HIPAA compliant with respect to the right to privacy.

The recruitment plan should specifically include the "site" or "sites" where the research will take place. Permission from the site(s) must be obtained if it is outside the PI's department. The permission should specifically state that permission is given for the research to be conducted at

the site and what specific activities would be taking place. The document should be signed by the individual who is authorized to give permission for the research to take place at that site. Hospital clinical sites can be used for recruitment purposes by various departments from throughout the University although permission must be obtained first before recruitment activities can begin.

Stony Brook participates in "ResearchMatch", a national research volunteer registry. Details for use of this recruitment tool are available in Section 17.13.

*NOTE: See Section 3.9.7 for a discussion of the IRB review of **advertisements**, and Section 3.9.8 for a discussion of the IRB review of **payments**.*

3.8.3 Informed Consent

The IRB will ensure that informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116 and 21 CFR 50.20 (when applicable). In addition, the IRB will ensure that informed consent will be appropriately documented in accordance with, and to the extent required by 45 CFR 46.117 and 21 CFR 50.27 (when applicable). See Section 5 below for detailed policies on informed consent.

3.8.4 Data Safety Monitoring

For all research that is more than minimal risk, the investigator must submit a data safety-monitoring plan. The initial plan submitted to the IRB should describe the procedures for safety monitoring (including what data will be collected, how it will be collected and by whom), reporting of adverse events and/or unanticipated problems involving risks to subjects or others, descriptions of interim safety reviews and the procedures planned for transmitting the results to the IRB. This description should include information regarding an independent Data and Safety Monitoring Board (DSMB), if one exists, or an explanation why an independent data safety monitor is not necessary.

The IRB determines whether the data safety-monitoring plan makes adequate provision for monitoring the data to ensure the safety of subjects. The overall elements of the monitoring plan may vary depending on the potential risks, complexity, and nature of the research study. The method and degree of monitoring needed is related to the degree of risk involved. Monitoring may be conducted in various ways or by various individuals or groups, depending on the size and scope of the research effort. These exist on a continuum from monitoring by the principal investigator in a small phase I study to the establishment of an independent data and safety monitoring board for a large phase III clinical trial.

The factors the IRB will consider in determining whether the safety-monitoring plan is adequate for the research are as follows:

1. Monitoring is commensurate with the nature, complexity, size and risk involved.
2. Monitoring is timely. Frequency should commensurate with risk. Conclusions are reported to the IRB.
3. For low risk studies, continuous, close monitoring by the study investigator or an independent individual may be an adequate and appropriate format for monitoring, with prompt reporting of toxicity to the IRB, sponsor and regulatory bodies as appropriate. For an individual Safety Monitor the plan must include:

- Parameters to be assessed;
- Mechanism to assess the critical efficacy endpoints at intervals in order to determine when to continue, modify, or stop a study;
- Frequency of monitoring; and
- Procedures for reporting to the IRB.

4. For a Data Safety Monitoring Board, the plan must include:

- The name of the Data Safety Monitoring Board;
- Where appropriate, independent status from the sponsor;
- Availability of written reports;
- Composition of the monitoring group (if a group is to be used): experts in all scientific disciplines needed to interpret the data and ensure patient safety. Clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease and treatment under study should be part of the monitoring group or be available if warranted;
- Frequency and content of meeting reports;

The frequency and character of monitoring meetings (e.g., open or closed, public or private).In general, it is desirable for a Data and Safety Monitoring Board (DSMB) to be established by the study sponsor for research that is blinded, involves multiple sites, involves vulnerable subjects, or employs high-risk interventions. For some studies, the National Institutes of Health (NIH) require a DSMB. The IRB has the authority to require a DSMB as a condition for approval of research where it determines that such monitoring is needed. When DSMBs are utilized, the IRB conducting continuing review of research may rely on a current statement from the DSMB indicating that it has and will continue to review study-wide AEs, interim findings, and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB.

3.8.5 Privacy and Confidentiality

The IRB will determine whether adequate procedures are in place to **protect the privacy** of subjects and to **maintain the confidentiality of the data**.

Definitions

Privacy: having control over the extent, timing, and circumstances of sharing oneself (physically, behaviorally, or intellectually) with others.

Confidentiality: methods used to ensure that information obtained by investigators about their subjects is not improperly divulged.

Private information: 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: where the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

3.8.5.1 Privacy

The IRB must determine whether the activities in the research constitute an invasion of privacy. In order to make that determination, the IRB must obtain information regarding how the investigators are getting access to subjects or subjects' private, identifiable information and the subjects' expectations of privacy. Investigators must have appropriate authorization to access subjects or subject information.

In developing strategies for the protection of subject privacy, consideration should be given to:

1. Methods used to identify and contact potential subjects.
2. Settings in which an individual will be interacting with an investigator.
3. Appropriateness of all personnel present for research activities.
4. Methods used to obtain information about subjects and the nature of the requested information.
5. Information that is obtained about individuals other than the "target subjects," and whether such individuals meet the regulatory definition of "human subject" (e.g., a subject provides information about a family member for a survey).
6. How to access the minimum amount of information necessary to complete the study.

3.8.5.2 Confidentiality

Confidentiality and anonymity are not the same. If anyone, including the investigator, can readily ascertain the identity of the subjects from the data, then the research is not anonymous and the IRB must determine if appropriate protections are in place to minimize the likelihood that the information will be inappropriately divulged. The level of confidentiality protections should be commensurate with the potential of harm from inappropriate disclosure.

At the time of initial review, the IRB ensures that the confidentiality of research subject data is protected. The IRB assesses whether there are adequate provisions to maintain confidentiality. The IRB does this through the evaluation of the methods used to obtain information:

1. About subjects;
2. About individuals who may be recruited to participate in studies;
3. The use of personally identifiable records; and
4. The methods to protect the confidentiality of research data.

The PI will provide the information regarding confidentiality of research subjects at the time of initial review through the completion of the application, any necessary HIPAA Forms, research protocol, and/or other submitted, applicable materials. The IRB will review all information received from the PI and determine whether or not confidentiality of research subject data is sufficiently protected. In some cases, the IRB may also require that a Certificate of Confidentiality be obtained to additionally protect research data.

In reviewing confidentiality protections, the IRB shall consider the nature, probability, and magnitude of harm that would be likely to result from a disclosure of collected information outside the research. It shall evaluate the effectiveness of proposed de-identification techniques, coding systems, encryption methods, storage facilities, access limitations, and other relevant factors in determining the adequacy of confidentiality protections.

3.8.6 Vulnerable Populations

At the time of initial review, the IRB will consider the scientific and ethical reasons for including vulnerable subjects in research. The IRB may determine and require that, when appropriate, additional safeguards are put into place for vulnerable subjects, such as those without decision-making capacity. The adequacy of those safeguards will be confirmed at the time of continuing review.

For an extensive discussion about the IRB's review and approval process for individual populations of vulnerable subjects, please refer to Section 6.

3.9 Additional Considerations during IRB Review and Approval of Research

3.9.1 Determination of Risk

At the time of initial and continuing review, the IRB will make a determination regarding the risks associated with the research protocols. Risks associated with the research will be classified as either "minimal" or "greater than minimal" based on the "absolute" interpretation of minimal risk. The meeting minutes will reflect the IRB's determination regarding risk levels. If risk is deemed minimal, the IRB will additionally vote to determine if subsequent review of the study may be conducted via the expedited review process.

3.9.2 Period of Approval

At the time of initial review and at continuing review, the IRB will make a determination regarding the frequency of review of the research protocols. All protocols will be reviewed by the IRB at intervals appropriate to the degree of risk but no less than once per year. For research subject to the Common Rule, the IRB will conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year, except as described elsewhere in these SOPs;

In some circumstances, a shorter review interval (e.g. biannually, quarterly, or after accrual of a specific number of subjects) may be required (see below). The meeting minutes will reflect the IRB's determination regarding review frequency.

3.9.2.1 Review More Often Than Annually

Certain variables may be considered by the IRB in determining those studies that require review more often than annually. For example:

- Significant risk to research subjects (e.g. death, permanent or long lasting disability or morbidity, severe toxicity) without the possibility of direct benefit to the subjects;
- The inclusion of vulnerable populations where, even in the presence of possible direct benefit, there is also a possibility of significant risk associated with the research procedures.
- A history of serious or continuing non-compliance on the part of the PI.
- The likely medical condition of the proposed subjects.
- The novelty of the research making unanticipated adverse events more likely.
- Any other factors that the IRB deems relevant.

In specifying an approval period of less than one year, IRB may define the period with either a time interval or a maximum number of subjects to be either studied or enrolled. If a maximum number of subjects studied or enrolled is used to define the approval period, it is understood that the approval period in no case can exceed one (1) year unless the study does not require continuing review. If an approval period of less than one year is specified by the IRB for research that is subject to continuing review, the reason for more frequent review must be documented in the minutes or the reviewer checklist.

3.9.3 Independent Verification That No Material Changes Have Occurred

The IRB recognizes that protecting the rights and welfare of subjects sometimes requires that the IRB verify independently, utilizing sources other than the investigator, that no material changes since previous IRB review have occurred. Independent verification from sources other than the investigator may be necessary at times, for example, in cooperative studies or other multi-center research.

The IRB will determine the need for verification from outside sources on a case-by-case basis. The following factors will be considered when determining which studies require independent verification. This content was updated based upon updates to AAHRPP's Evaluation Instrument. AAHRPP's listing of considerations (#'s 1-7) are required for FDA-regulated research:

1. The nature, probability, and magnitude of anticipated risks to subjects;
2. The degree of uncertainty regarding the risks involved;
3. Whether the research involves novel therapies or procedures;
4. The vulnerability(ies) of the subject population;
5. The projected rate of enrollment;
6. The experience and expertise of the investigators;
7. The IRB's previous experience with the investigators or the sponsor (e.g., compliance history, complaints from subjects, etc.);
8. The probable nature and frequency of changes that may ordinarily be expected in the type of research;
9. Whether the research undergoes routine independent monitoring;
10. Whether concerns about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources; and
11. Any other factors that suggest independent verification is warranted.

If any material changes have occurred without IRB review and approval, the IRB will assess the issue in accordance with procedures for noncompliance detailed in Section 10.

3.9.4 Consent Monitoring

In reviewing the adequacy of informed consent procedures, the IRB routinely monitors consent processes of approved studies (see Section 5.9 for details). It may also, on occasion, determine that special monitoring of the consent process by an impartial observer (consent monitor) is required in order to reduce the possibility of coercion and undue influence.

Such monitoring may be particularly warranted where the research presents significant risks to subjects, or if subjects are likely to have difficulty understanding the information to be provided. Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with a particular investigator or a research project.

See Section 5.9 for a detailed discussion of consent monitoring.

3.9.5 Investigator Conflicts of Interest

All investigators are informed of University Policy P209 and disclosures that must be completed for all investigators on the study. Where disclosure is made that an investigator has significant financial interests, the IRB and the University COI Committee will each independently assess the existence of a financial conflict of interest, and if yes, whether or not the conflict can be managed, in accordance with PHS policy. The IRB's contribution to a resulting conflict management plan will specifically focus on the protection of human subjects. Where there is a conflict between the IRB and COI committees regarding the adequacy of a particular management plan, the IRB decision will be final. (See Section 14 for a detailed discussion of Conflict of Interest).

3.9.6 Significant New Findings

During the course of research, significant new knowledge or findings about the medication or test article and/or the condition under study may develop. The PI must report any significant new findings to the IRB and the IRB will review them with regard to the impact on the subjects' rights and welfare. Since the new knowledge or findings may affect the risks or benefits to subjects or subjects' willingness to continue in the research, the IRB may require, during the ongoing review process, that the PI contact the currently enrolled subjects to inform them of the new information via a consent addendum. The IRB will communicate this to the PI. The informed consent should be updated and the IRB may require that the currently enrolled subjects be re-consented, acknowledging receipt of this new information and for affirming their continued participation.

3.9.7 Advertisements

The IRB must approve any and all advertisements prior to posting and/or distribution for studies that are conducted under the purview of the IRB. The following will be reviewed:

1. The information contained in the advertisement;
2. The mode of its communication;
3. The final copy of printed advertisement; and/or
4. The final audio/video taped advertisements.

This information should be submitted to the IRB with the initial application or as an addendum to the protocol.

The IRB reviews the material to assure that the material is accurate and is not coercive or unduly optimistic, creating undue influence to the subject to participate, which includes, but is not limited to:

1. Statements implying a certainty of favorable outcome or other benefits beyond what was outlined in the consent document and the protocol.
2. Claims, either explicitly or implicitly, that the drug, biologic or device was safe or effective for the purposes under investigation
3. Claims, either explicitly or implicitly, that the test article was known to be equivalent or superior to any other drug, biologic or device
4. Using terms like “new treatment,” “new medication,” or “new drug” without explaining that the test article was experimental.
5. Promising “free medical treatment” when the intent was only to say subjects will not be charged for taking part in the investigation.
6. Emphasis on payment or the amount to be paid, such as bold type or larger font on printed media.
7. The inclusion of exculpatory language.

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

1. The name and address of the clinical investigator and/or research facility.
2. The condition being studied and/or the purpose of the research.
3. In summary form, the criteria that will be used to determine eligibility for the study.
4. The time or other commitment required of the subjects.
5. The location of the research and the person or office to contact for further information.

6. A clear statement that this is research and not treatment.
7. A brief list of potential benefits (e.g. no cost for a health exam).
8. Advertisements will not include compensation for participation in a trial offered by a sponsor to involve a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

Once approved by the IRB, an advertisement cannot be altered or manipulated in any way without prior the IRB approval.

3.9.8 Payment to Research Subjects

Payment to research subjects may be an incentive for participation or a way to reimburse a subject for travel and other experiences incurred due to participation. However, payment for participation is not considered a research benefit. Regardless of the form of remuneration, investigators must take care to avoid coercion of subjects. Payments should reflect the degree of risk, inconvenience, or discomfort associated with participation. The amount of compensation must be proportional to the risks and inconveniences posed by participation in the study.

Investigators who wish to pay research subjects must indicate in their research project application the justification for such payment. Such justification should:

1. Substantiate that proposed payments are reasonable and commensurate with the expected contributions of the subject;
2. State the terms of the subject participation agreement and the amount of payment in the informed consent form; and
3. Substantiate that subject payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure on the individual to volunteer for the research study.

The IRB must review both the amount of payment and the proposed method of disbursement to assure that neither entails problems of coercion or undue influence.

Credit for payment should accrue and not be contingent upon the subject completing the entire study. The IRB does not allow the entire payment to be contingent upon completion of the entire study. Any amount paid as bonus for completion of the entire study should not be so great that it becomes coercive.

The consent form must describe the terms of payment and the conditions under which subjects would receive partial payment or no payment (e.g. if they withdraw from the study before their participation is completed).

Acting as an agent for the Research Foundation (RF) of SUNY, the Office of Grants Management (OGM) requires certain identifying information (name, address, SSN#) to issue checks, cash, or gift certificates to subjects. Payments to subjects are entered into the RF's Oracle system, for tracking purposes. All withholdings/payments made will be reported to those in charge of taxes (IRS) by the Research Foundation. If an individual subject reaches or exceeds $600 during the calendar year, the RF issues a 1099 to the individual. The consent form must inform subjects that are U.S. citizens or resident aliens that if they will be paid more than $600 in a year as a research subject, their social security number will be reported to the IRS, and they will have to pay taxes on that money. Subjects that are non-resident aliens will have a 30% tax withholding from their payment.

For certain sensitive research, e.g. HIV+ patients, the investigator may opt to use a payment form that only identifies the subject by a patient ID # (no name, address or SS# is identified). The PI is issued a cash advance from which the payments are made and the PI accepts the responsibility of tracking the amount of the payments during the calendar year to ensure compliance with IRS regulations. The consent form discloses the annual $600 criterion for payment of taxes. If the subject is a non-resident alien, the individual is subject to a 30% tax withholding.

3.9.9 Recruitment Incentives

Payment from sponsors for subject recruitment should be primarily based on expenses incurred by the site to run subjects through the course of the study. They must not place subjects at risk of coercion or undue influence or cause inequitable selection. Payment in exchange for referrals of prospective subjects from investigators (physicians) (“finder’s fees”) is not permitted. Payments that are designed to accelerate recruitment by being tied to the rate or timing of enrollment (“bonus payments”) are not permitted.

3.9.10 Compliance with all Applicable State and Local Laws

The IRB follows and must adhere to all applicable state and local laws in the jurisdictions where the research is taking place. The HRPP and the IRB rely on SUNY Counsel for the interpretation and application of New York State laws and the laws of any other jurisdiction where research is conducted as they apply to human subject research.

All consent forms must be consistent with applicable state and local laws.

3.10 Possible IRB Actions

In conducting its review of research, the IRB may take any of the following actions. With the exception of disapproval, the actions listed below may be used for either expedited or convened

board review, including limited IRB review. An action of disapproval can only be taken at a convened IRB meeting.

Approval: The study is approved as submitted.

Modifications Required in Order to Secure Approval: The requested revisions are prescriptive, requiring concurrence by the PI (e.g., the submission requires minor revisions, such as wording changes, with replacement language provided or confirmation by the PI of the IRB's understanding of a particular issue). If the study is returned with substantive changes or requirements, requests for more information for IRB consideration, and other issues **related to the criteria for approval** the changes require review and approval by the convened IRB.

For studies undergoing full review, the needed revisions are agreed upon at the meeting; for those undergoing expedited review, they are designated by the reviewer(s).

In order to receive approval for a protocol requiring modifications:

- For full review studies, the investigator's response, the revised protocol and the previously submitted protocol is triaged by IRB staff to assess if a final reviewer was specifically assigned at the meeting in which the study was reviewed. If not, IRB staff who are IRB members will either conduct final review or share with either the IRB Chair, or a subcommittee (e.g. primary and/or secondary reviewers) for review. The reviewer(s) may approve the study upon receipt and approval of the revisions without further action by the IRB.
- For expedited studies, the investigator's response, and all other materials will either be returned to the original reviewer, or handled by IRB staff.

Approval of the protocol application will not be granted and certification will not be issued until all deficiencies, if any, are corrected to the satisfaction of the final reviewer(s).

The outcome of the IRB's or expedited reviewer's deliberations is once again communicated to the investigator in writing. These deliberations are also documented in the minutes and in the electronic study file for full and expedited studies, respectively.

Note: For full review, the expiration date for the protocol is calculated based on the date that the convened IRB reviewed the protocol and NOT on the final approval date.

Deferral (Expedited Review): If an expedited reviewer defers a study, the IRB Staff will place it on the agenda for the next IRB meeting.

Deferral (Full Review): A deferral means that substantive changes regarding the submission must be addressed. This action is taken if substantive modification or clarification is required, or insufficient information is provided to judge the protocol application adequately (e.g., the risks and benefits cannot be assessed with the information provided). The IRB approval of the proposed research must not occur until subsequent review of the material the PI submitted by the convened IRB.

In order to receive approval for a protocol deferred for substantive issues:

- For full review, the investigator's response must be submitted for review at a subsequent, convened meeting of the same IRB. The ORC provides the IRB with the investigator's response. All prior and new materials are available to all members via the electronic management system. The item is placed on the agenda for re-review at the next meeting.

Approval of the protocol application will not be granted and certification will not be issued until all deficiencies, if any, are corrected to the satisfaction of the IRB.

Studies that have been deferred twice and during the review appear to be receiving a third deferral should be considered for a vote of "disapproval" unless the IRB determines that issues related to the deferral can be corrected.

The outcome of the IRB's deliberations is communicated to the investigator in writing.

The IRB's determination concerning the subsequent amended submission will be documented in the minutes of the IRB meeting.

Disapproval: The IRB has determined that the research cannot be conducted at the University or by employees or agents of the University or otherwise under the auspices of the University. Disapprovals must be determined at meetings of the full committee; they cannot be determined at the level of expedited review.

Tabled: The IRB is unable to review the research at the convened meeting (e.g., due to incomplete submission, loss of quorum, etc.).

3.11 Study Suspension, Termination

3.11.1 Suspension/Termination

IRB approval may be suspended or terminated if research is not being conducted in accordance with the IRB or regulatory requirements or that has been associated with unexpected problems or

serious harm to subjects. (See Section 8 for a discussion of unexpected problems and Section 10 for a discussion of non-compliance). The IRB's authority to suspend or terminate research applies to all research subject to IRB approval, including exempt research with limited IRB review and research for which continuing review is no longer required.

Suspension of IRB approval is a directive of the convened IRB, IRB Chair, AVP-RC, or the IO to temporarily stop some or all previously approved research activities. Suspended protocols remain open and require continuing review. Termination of IRB approval is a directive of the convened IRB to permanently stop all activities in a previously approved research protocol. Terminated protocols are considered closed and no longer require continuing review.

The IRB shall notify the PI and the PI's department chair in writing of such suspensions or terminations and shall include a statement of the reasons for the IRB's actions. The terms and conditions of the suspension must be explicit. The investigator shall be provided with an opportunity to respond in person or in writing.

The IRB Chair, AVP-RC, or IO may suspend research to ensure protection of the rights and welfare of subjects. Suspension or IRB approval made by these individuals **must** be reported to a meeting of the convened IRB for further deliberation and actions.

Research may only terminated by the convened IRB. Terminations of protocols approved under expedited review must be made by the convened IRB.

When study approval is suspended or terminated by the convened IRB or an authorized individual, consideration will also be made of actions needed to protect the rights and welfare of currently and/or formerly enrolled subjects, e.g., informing them of the suspension/ termination, procedures that are needed to withdraw them safely such as transferring currently enrolled subjects to another investigator; making arrangements for care or follow-up outside the research; allowing continuation of some research activities under the supervision of an independent monitor; or requiring or permitting follow-up of subjects for safety reasons.

If follow-up of subjects for safety reasons is permitted/required by the convened IRB or individual ordering the suspension or termination, the convened IRB or individual ordering the suspension or termination will require that the subjects should be so informed, and that any adverse events/outcomes be reported to the IRB and the sponsor.

The investigator MUST continue to provide reports on adverse events and unanticipated problems to both the IRB and sponsor just as if there had never been a suspension (i.e. all events that need to be reported during a study need to continue to be reported during the suspension period).

Refer to Section 11 for the University's requirements for reporting suspensions or terminations to external agencies.

3.12 Continuing Review

For research subject to the Common Rule, the IRB will conduct continuing review of ongoing research requiring review by the convened IRB at intervals that are appropriate to the level of risk of the research, but not less than once per year, except as described below. The date by which continuing review must occur will be recorded in the IRB electronic management system and on initial and continuing review approval letters.

Unless an IRB determines otherwise, continuing review of research subject to the Common Rule is not required in the following circumstances:

- Research eligible for expedited review in accordance with 45 CFR 46.110;
- Research reviewed by the IRB in accordance with the limited IRB review described in Section 3.5.2;
- Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
  - Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
  - Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

Studies that fall into these categories and are determined to not require continuing review are still subject to prompt reporting requirements (e.g., proposed amendments, unanticipated problems involving risk to subjects or others, protocol deviation/violations/non-compliance). **They will also require submission of a status report** every two years that will collect information regarding the status of the research activity. Investigators will receive courtesy reminder e-mail notices for completion of the status report. ORC staff will review the report for compliance with institutional policies (verification of human subjects training, COI review, etc). Failure to submit a status report as required will constitute non-compliance with SBU's HRPP policy and may result in suspension of the study until compliance with this policy is confirmed.

Studies that fall into these categories may be determined to require continuing review. For example, the IRB may determine that continuing review is required when:

1. Required by other applicable regulations (e.g., FDA);
2. Required by the terms of a grant, contract, or other agreement
3. The research involves topics, procedures, or data that may be considered sensitive or controversial;

4. The research involves particularly vulnerable subjects or circumstances that increase subjects' vulnerability;
5. An investigator has minimal experience in research or the research type, topic, or procedures; and/or
6. An investigator has a history of noncompliance

When the IRB determines that continuing review is required for such research, it will document the rationale in the IRB record and communicate the requirement to the investigator in the IRB determination letter.

There is no exception to the requirement for continuing review in FDA regulations. The IRB will conduct continuing review of ongoing FDA-regulated research, and any research where it is required as a condition of funding or contractually, at intervals that are appropriate to the level of risk of the research, but not less than once per year, as long as the research remains active. The date by which continuing review must occur will be recorded in the IRB electronic management system and on initial and continuing review approval letters.

3.12.1 Approval Period

Determination of the approval period is made by the IRB on a protocol-by-protocol basis at the time of initial review and at continuing review. For research subject to the Common Rule, the IRB will conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk of the research, but not less than once per year, except as described elsewhere in these SOPs;

For each initial or continuing approval, the IRB will indicate an approval period with an expiration date specified. The IRB approval is considered to have lapsed at midnight on the expiration date of the approval. For a study reviewed by the convened the IRB, the approval begins on the date that the IRB conducts its final review of the study; that is, the date that the convened IRB approves the research or the date that a final reviewer approves the study following a 'modifications required' determination, for non-substantive issues by the full committee. The expiration date is no later than one year from the date that the full committee last reviewed the study.

For a study subject to the common rule and approved under expedited review, the approval period begins on the date the IRB Chair or the IRB member(s) designated by the IRB Chair gives final approval to the protocol, and the expiration date is no later than one year from date of final approval.

The approval date and approval expiration date are clearly noted on all the IRB letters sent to the PI and must be strictly adhered to. Investigators should allow sufficient time for development and review of renewal submissions. Electronic courtesy reminder notices are sent 90, 60, and 30 days prior to expiration, but it remains the PI's responsibility to maintain continued approval for their studies.

Review of an amendment/modification to a protocol does not alter the date by which continuing review must occur.

The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of the IRB approval. Therefore, continuing review and re-approval of research must occur by midnight of the date when the IRB approval expires.

3.12.2 Continuing Review Process

In conducting continuing review of research not eligible for expedited review, IRB members will be directed to conduct a substantive review of the materials submitted for continuing review along with all study history residing in the electronic management system. Primary and secondary reviewers will lead the discussion at the convened meeting regarding study, including its aims, progress, history, and assessment of whether or not the approval criteria continue to be met.

3.12.3 Expedited Review of Continuing Studies

In conducting continuing review under the expedited review process, the reviewers have access to all materials submitted for continuing review as well as all study history residing in the electronic management system. Reviewers will complete the Approval Criteria Worksheet for Expedited Reviews, including assessment that the regulatory criteria for expedited review and IRB approval continue to be met, with indication of approval, required modifications or 'deferred to full committee'. If the research no longer requires continuing review under the Common Rule but the IRB reviewer determines that continuing review is required, the reviewer shall document the rationale in the checklist.

Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, unless it is not subject to FDA regulation, and has progressed to the point that it involves only one or both of the following:

- Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
- Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care;

and in limited circumstances described by expedited review categories (8) and (9).

3.12.4 Continuing Review of Exempt Studies

IRB staff will not provide a continuing review of an exempt study once the study has received an exempt determination.

3.12.5 What Happens if there is a Lapse in Continuing Review?

The regulations permit no grace period or approval extension after approval expiration. Research that continues after the approval period has expired is research conducted without IRB approval and will be handled in accordance with the Noncompliance SOP. If the continuing review does not occur within the timeframe set by the IRB, all research activities must stop, including recruitment (media advertisements must be pulled), enrollment, consent, interventions, interactions, and data collection, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. **This will occur even if the investigator has provided the continuing information before the expiration date. Therefore, investigators must allow sufficient time for IRB review and approval before the expiration date**.

The electronic management system notifies the investigator of the expiration of approval with notice that research activities must stop. With this notice, the PI is advised to immediately submit to the ORC a list of any currently enrolled research subjects for whom suspension of the research would cause harm. Enrollment of new subjects cannot occur, and continuation of research interventions or interactions for already enrolled subjects should only continue, when the IRB or the IRB Chair finds that it is in the best interest of the individual subjects to do so.

Once approval has expired, the IRB review and re-approval must occur prior to re-initiation of the research. If the study approval has lapsed more than 90 days and the PI has not provided the required continuing review information, the PI may be required to submit a new application to the IRB for review and approval. If the study approval has lapsed 90 days or less and the PI provides the required continuing review information, the existing protocol may be reviewed for consideration of continued IRB approval.

If the IRB requires modifications at the time of continuing review, and the approval expires before the IRB has reviewed and approved the PI response, all activities involving human subjects or their tissue/data must be stopped as described above.

3.13 Amendment of an Approval Protocol

Investigators may wish to modify or amend their approved research. Investigators must seek approval from the IRB before making any changes, no matter how minor, in approved research unless the change is necessary to eliminate an immediate hazard to the subject (in which case the IRB must be notified immediately).

Modifications may be approved if they are within the scope of what the IRB originally authorized. For example, if an investigator wishes to add a population to an existing study, but not alter the study procedures or purpose, a modification request is usually appropriate. Likewise, modifying a procedure without changing the study's purpose or study population may also be appropriate. If, however, the investigator wishes to alter the original aims (scope), purpose, or intent of the research, he or she will likely need to submit a new application for human subjects approval.

Investigators must submit to the IRB any and all revised documents that are impacted by the modification, as well as a justification and summary of changes, and track-changed materials whenever possible.

IRB staff will determine whether the proposed changes may be approved through an expedited review process (if the changes are minor and not increasing risk), or whether the modification warrants full board review. If expedited, the IRB reviewer(s) has the ultimate responsibility to determine that the proposed changes may be approved through the expedited review procedure and, if not, must defer the protocol to full board review.

3.13.1 Expedited review of Protocol Modifications

The IRB may use expedited review procedures to review minor changes in ongoing previously-approved research during the period for which approval is authorized. An expedited review may be carried out by the IRB Chair and/or designee(s) among the IRB members.

The reviewer(s) complete the Amendment Review Sheet for IRB Members to determine whether the modifications meet the criteria allowing review of the amendment using the expedited procedure, and if so, whether the research with the proposed modifications continues to meet the regulatory criteria for approval.

The reviewer(s) will also consider whether information about those modifications might relate to subjects' willingness to continue to take part in the research and if so, whether to provide that information to subjects

3.13.2 Full Board Review of Protocol Modifications

When a proposed change in a research study is not minor (e.g. procedures involving increased risk or discomfort are to be added), then the IRB must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB should be promptly informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the subjects' continued welfare. IRB members must consider whether the incident was an “unanticipated problem involving risks to subjects and/or others”; whether the protocol should be revised; and whether the consent form should include revisions.

All documents provided by the investigator are accessible to all IRB members.

At the meeting, the primary reviewer presents an overview of the changes and leads the IRB through the completion of the regulatory criteria for approval. The IRB will determine whether the research with the proposed changes continues to meet the regulatory criteria for approval.

When the IRB reviews changes to previously approved research, the IRB consider whether information about those modifications might relate to subjects’ willingness to continue to take part in the research and if so, whether to provide that information to subjects.

3.14 Closure of Protocols

The completion or termination of the study, whether premature or not, is a change in activity and should be reported to the IRB via the electronic management system. Although subjects will no longer be "at risk" under the study, a final report to the IRB allows it to close its files as well as provides information that may be used by the IRB in the evaluation and approval of related studies.

3.15 Reporting IRB Actions

Barring extraordinary circumstances, all the IRB action letters are prepared by IRB staff in the electronic management system and accessed by the PI and research team within ten (10) working days of receipt of member review (for expedited studies) or IRB meeting in which the study was reviewed (for full review studies). For an approval, along with written notification of approval, a copy of the approved consent/permission/assent document(s) containing the stamped approval with the dates of the approval and expiration on each sheet will be uploaded. Stamping of expiration dates on the consent form will not be required for studies approved under the new Common Rule, however, the study application will require. For required modifications or deferrals,

the notification will include the information that is required and the basis for requiring those modifications. For a disapproval, termination or suspension, the notification will include the basis for making that decision.

All correspondence between the IRB and investigators are retained in the electronic management system.

The IRB reports its findings and actions to the University in the form of its minutes, which are stored permanently and securely in the ORC office, and in the electronic management system.

3.16 Appeal of the IRB Decisions

When a protocol presented at a convened IRB meeting is disapproved, deferred or requires modifications, the IRB will notify the PI in writing about the specific deficiencies and the modifications that are necessary for appropriate IRB approval. The IRB shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in writing.

In cases where there is disagreement between the IRB and the PI regarding the nature and extent of the requested changes and these disagreements cannot be resolved amicably in an informal manner, the PI and/or the IRB may make an appeal to the IO for a resolution of the matter. The IO may organize a meeting to help facilitate discussion between the IRB and the PI. While the IO may provide input and make recommendations to the IRB for expeditious resolution of the matter, final recommendations for approval remain under the purview of the IRB.

4 IRB Documentation and Records

4.1 Policy

The University shall prepare and maintain adequate documentation of the IRB's activities. All records must be accessible for inspection and copying by authorized representatives of the FDA, OHRP, sponsors, and other authorized entities at reasonable times and in a reasonable manner.

4.2 IRB Records

The IRB records include, but are not limited to:

1. Written operating procedures.
2. IRB membership rosters.

3. Training records. The ORC maintains accurate records listing research investigators, IRB members, and IRB staff that have fulfilled the facility's human subject training requirements.
4. IRB correspondence (other than protocol related).
5. IRB Study Files (See Section 4.3 for information included in study files)
6. Documentation of Emergency Exemption from Prospective IRB Approval. (21 CFR 56.104(c)).
7. Documentation of Exceptions from Informed Consent Requirements for Emergency Use of a Test Article ((21 CFR 50.23).
8. Documentation of exemptions, including when limited IRB review is a condition of exemption.
9. Documentation of convened IRB meetings minutes
10. Documentation of review by an external IRB when appropriate.
11. Documentation of IRB reliance and cooperative review agreements.

For nonexempt research involving human subjects covered by the Common Rule (or exempt research for which limited IRB review applies) that takes place at an institution in which IRB oversight is conducted by an IRB that is not operated by the institution, the institution and the organization operating the IRB shall document the institution's reliance on the IRB for oversight of the research and the responsibilities that each entity will undertake to ensure compliance with the requirements of this policy (e.g., in a written agreement between the institution and the IRB, by implementation of an institution-wide policy directive providing the allocation of responsibilities between the institution and an IRB that is not affiliated with the institution, or as set forth in a research protocol).

12. Federal Wide Assurances;
13. Federal IRB registration;
14. Protocol violations submitted to the IRB
15. Quality assurance reviews.
16. Documentation of complaints and any related findings and/or resolution.

4.3 IRB Study Files

ORC will maintain an electronic study file for each IRB study submission that is submitted via the electronic management system for review.

All communications to and from the IRB are maintained. Depending on the type of communication, maintenance may be via the electronic management system, IRB staff e-mail, or paper. IRB study files include, but are not limited to:

1. Protocol and all other documents submitted as part of a new protocol application. This includes recruitment materials and the investigator's brochure (if any).

2. Protocol and all other documents submitted as part of a request for continuing review/termination of research application. This also includes progress reports, statements of significant new findings provided to subjects, reports of injuries to patients.
3. Documents submitted and reviewed after the study has been approved, including reports of modifications to research/amendments and adverse event reports.
4. Copy of the IRB-approved Consent/permission/assent forms
5. Sponsor-approved (including DHHS) sample consent form document and protocol, when they exist.
6. IRB reviewer forms (when expedited review procedures are used)
7. Documentation of type of IRB review.
8. For expedited review, documentation of risk determination, criteria for approval, period of approval (when continuing review is required), any determinations required by the regulations and protocol-specific findings supporting those determinations, including: waiver or alteration of the consent process, research involving pregnant women, fetuses, and neonates, research involving prisoners, and research involving children. Any actions taken by the reviewer.
9. For expedited review, the rationale for an expedited reviewer's determination under 45 CFR 46.110(b)(1)(i) that research appearing on the expedited review list described in 45 CFR 46.110(a) is no more than minimal risk.
10. Documentation of all IRB review actions, including the rationale for conducting continuing review of research that otherwise would not require continuing review and criteria for approval.
11. Notification of expiration of IRB approval to the PI and instructions for submitting relevant continuing review materials.
12. Notification of suspension of research.
13. Correspondence pertaining to appeals.
14. Copies of approval letters and forms that describe what PI must have before beginning the study.
15. IRB correspondence to and from research investigators.
16. All other IRB correspondence related to the research.
17. Reports of unanticipated problems involving risk to subjects or others, non-compliance (and whether non-compliance is serious and/or continuing), and adverse events.
18. Documentation of audits, investigations, reports of external site visits.
19. Scientific evaluations, if any, beyond the scientific merit attestations provided by departmental chairs/review committees.
20. Data and safety monitoring reports, if any.
21. Justification for an exempt determination.

4.4 IRB Minutes

Proceedings must be written and available for the IRB Chair's review prior to the next regularly scheduled IRB meeting date. The IRB minutes, once approved, may not be altered by any persons of authority without the concurrence and approval of the convened IRB.

Minutes of the IRB meetings must contain sufficient detail to show:

1. Attendance.

    a. Each member's (or alternate's) full name;

    b. Each member's (or alternate's) representative capacity (e.g., scientist, non-scientist, unaffiliated, member who represents the general perspective of research subjects) (a roster sheet will be attached to the minutes indicating the representative capacity for each IRB member)

    c. The names of members or alternate members who are participating through videoconference or teleconference and documentation that those attending remotely received all pertinent material prior to the meeting and were able to actively and equally participate in all discussions;

    d. Names of alternates attending in lieu of specified (named) absent members. (Alternates may substitute for specific absent members or categories of members only as designated on the official IRB membership roster);

    e. Names of any consultants present, a brief explanation of their expertise, and documentation to support that the consultant(s) did not vote;

    f. The names of non-members and guests in attendance, such as IRB staff, investigators, and study coordinators

The vote on each action will reflect those members present for the vote on that item. Members who recuse themselves because of conflict of interest are listed by name and the reason documented.

2. The presence of a quorum throughout the meeting, including the presence of one member whose primary concern is in a non-scientific area.
3. Business Items discussed.
4. Continuing Education.
5. Actions taken, including separate deliberations, actions, and votes for each protocol undergoing initial review, continuing review, or review of modifications by the convened the IRB. Documentation that the criteria for approval was met.

6. Votes on these actions (total number voting; number voting for; number voting against; number abstaining; number of those recused).
7. Basis or justification for these actions including required changes in research.
8. Basis for disapproving research.
9. Summary of controverted issues and their resolution. When controverted issues are different in the worksheet from the opinion of the IRB members, the members' decision regarding the controverted issue will be documented in the minutes. However, the reviewer worksheets documenting a difference of opinion from the IRB member will remain permanently with the file.
10. Approval period for initial and continuing approved protocols, when applicable, including identification of research that warrants review more often than annually and the basis for that determination.
11. The rationale for requiring continuing review of research that otherwise would not require continuing review
12. Risk level of initial and continuing approved protocols
13. Protocol-specific documentation that the research meets the required criteria [45 CFR 46.116(d)] when approving a consent procedure that does not include or that alters some or all of the required elements of informed consent, or when waiving the requirement to obtain an informed consent. This documentation may alternatively be available in a supporting meeting document ("Final Meeting Determination Supplement: CONSENT WAIVERS") available with the meeting minutes.
14. Protocol-specific documentation that the research meets the required criteria [45 CFR 46.117(c)] when the requirements for documentation of consent are waived. This documentation may alternatively be available in a supporting meeting document ("Final Meeting Determination Supplement: CONSENT WAIVERS") available with the meeting minutes. Supplemental documents are permanently part of the file.
15. When approving research that involves populations covered by Subparts B, C, or D of 45 CFR 46, the minutes and/or supporting meeting document(s) will document the IRB's justifications and findings regarding the determinations stated in the Subparts. These documents are: "Final Meeting Determination Supplement: Minors, Final Meeting Determination Supplement: Pregnant Women, or Final Meeting Determination Supplement: Prisoners". Alternatively, the IRB may cite concurrence with the justifications as presented by the investigator on submission materials (or as modified per the IRB).
16. Special protections warranted in for other groups of subjects who are likely to be vulnerable to coercion or undue influence, such as mentally disabled persons, or economically or educationally disadvantaged persons, regardless of source of support for the research.
17. The rationale for significant risk/non-significant risk device determinations.
18. Determinations of conflict of interest and review of management plans.

19. Identification of any research for which there is need for verification from sources other than the investigator that no material changes are made in the research.
20. A list of research approved since the last meeting utilizing expedited review procedures, including limited IRB review conducted using expedited procedures.
21. An indication that, when a IRB member has a conflicting interest (see Section 2.9) with the research under review, the IRB member was not present during the deliberations or voting on the proposal, and that the quorum was maintained.
22. Key information provided by consultants will be documented in the minutes or in a report provided by the consultant.
23. Justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document.

4.5 IRB Membership Roster

A membership list of the IRB members must be maintained. It must identify members sufficiently to describe each member's chief anticipated contributions to IRB deliberations. The list must contain the following information about members:

1. Name.
2. Earned degrees.
3. Affiliated or non-affiliated status (neither the member nor an immediate family member of the member may be affiliated with the University).
4. Employment or other relationship etween each IRB member and the organization.
5. Status as scientist or non-scientist (Per OHRP: “Members whose training, background, and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline should be considered a scientist, while members whose training, background, and occupation would incline them to view research activities from a standpoint outside of any biomedical or behavioral scientific discipline should be considered a nonscientist.”)
6. Indications of experience (specialties, etc.) sufficient to describe each member's chief anticipated contributions to the IRB deliberations.
7. Representative capacities of each IRB member; including which IRB member(s) is a prisoner representative, and which IRB members are knowledgeable about or experienced in working with children, pregnant women, adults with impaired decision-making capacity, and other subjects vulnerable to coercion or undue influence commonly involved in research at SBU;
8. Role on the IRB (Chair, Co-Chair, etc.).
9. Voting status (Any ex officio members are non-voting members).
10. Alternate members.

11. For alternate members, the primary member or class of primary members for whom the member could substitute.

The ORC must keep IRB membership list current but are not required to submit changes to the roster to the Office for Human Research Protections (OHRP), Department of Health and Human Services (DHHS).

4.6 Documentation of Exemptions

Documentation of verified exemptions consists of the reviewer's citation of a specific exemption category and written concurrence that the activity described in the investigator's request satisfies the conditions of the cited exemption category as detailed in Section 3.5.2. When an exemption includes limited IRB review, the documentation will include this fact and the IRB action taken on those aspects of the research subject to limited IRB review in accordance with the procedures described for the review procedures used (expedited or convened board) elsewhere in this policy.

4.7 Documentation of Expedited Reviews

IRB records for initial and continuing review by the expedited procedure must include the reviewer's verification that the study qualifies for expedited review including the specific permissible category(ies) or status as exempt but requiring limited IRB review, documentation that the activity satisfies the criteria for approval, the period of approval (when applicable), and any determinations required by the regulations including study-specific findings justifying the following determinations:

1. Approving a procedure which waives or alters the informed consent process;
2. Approving a procedure which waives the requirement for documentation of consent;
3. Approving research involving pregnant women, human fetuses, or neonates;
4. Approving research involving prisoners;
5. Approving research involving children.

4.8 Access to IRB Records

The IRB has policies and procedures to protect the confidentiality of research information:

1. All paper IRB records are kept secure in the ORC, which is closed and locked when unattended.
2. The University's IRB electronic management program, is hosted at a data center facility on the Main Campus. Facilities are secure, data is mirrored, and is backed up nightly. Authorized users have restricted access to the facility. Security precautions are state of the art. Security standards associated with user ids and passwords are in accordance with generally accepted

commercial and federal security. Certified SSL (256 bit Secured Socket Layer technology) encryption is standard for all web-based transmissions. Strict permission rules ensure that only approved individuals have access to the data.

3. Access to IRB records, whether paper or electronic, is limited to the IO, IRB Chair, IRB members, IRB Administrators, IRB staff, AVP-RC, authorized institutional officials, and officials of Federal and state regulatory agencies (OHRP, FDA). Appropriate accreditation bodies are provided access and may recommend additional procedures for maintaining security of IRB records. All other access to IRB records is limited to those who have legitimate need for them, as determined by the AVP-RC, or the IO.
4. Records are accessible for inspection and copying by authorized representatives of federal regulatory agencies during regular business hours.
5. Paper records may not be removed from the ORC office; however, the IRB staff will provide copies of records for authorized personnel if requested.
6. All other access to IRB study files, paper or electronic, is prohibited.

4.9 Record Retention

Records pertaining to IRB-approved research must be retained for a defined time period once the research is permanently closed.

Research is permanently closed if all of the following conditions are met:

- No new subjects will be enrolled; **and**
- There are no more interventions or interactions with enrolled subjects; **and**
- No further analysis of identifiable data/tissue will be conducted. Either analyses are complete or data/tissue have been permanently de-identified (i.e., with all identifiers and keys to codes destroyed).

The time period during which records must be kept once the research is permanently closed depends on the study specifics:

- **For records that DO NOT include identifiable health information and are not subject to FDA regulation, contract or journal requirement:** Records relating to the research must be retained for at least 3 years after completion of the research.

- **For records that are subject to specific contract or journal requirements:** Records relating to the research must be retained per the stated contractual or journal obligation.

- If a protocol is cancelled without participant enrollment, IRB records are maintained for at least three years after cancellation

- **For records that DO include identifiable health information:** Records relating to the research must be retained for at least 7 years after completion of the research.

- **For Investigational New Drug (IND) research:** The FDA requires that sponsors and investigators retain "records and reports required by this part for 2 years after a marketing application is approved for the drug; or if an application is not approved for drug, until 2 years after shipment and delivery of the drug for investigational use is discontinued and the FDA so notified."

- **For Investigational Device Exemption (IDE) research:** The FDA requires the investigator or sponsor to maintain the records "for a period of 2 years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol."

- **For research funded by industry or private foundations:** The investigator should maintain the records for either the length of time required by the sponsor, or three (3) years, whichever is longer.

5 Obtaining Informed Consent from Research Subjects

5.1 Policy

No investigator conducting research under the auspices of the University may involve a human being as a subject in research without obtaining the legally effective informed consent of the subject or the subject's legally authorized representative unless a waiver of consent has been approved by the IRB in accordance with Section 5.8 of these procedures. Except as provided in Section 5.12 of these procedures, informed consent must be documented by the use of a written consent form approved by the IRB (See Section 5.6).

The Office for Human Research Protection (OHRP) and Food and Drug Administration (FDA) regulations state that designation of a subject's legally authorized representative is to be determined by "applicable law" (45 C.F.R. 46.102(c); 21 C.F.R. 50.3(l)), which typically means state or local statutes, regulations or cases. OHRP guidance states that it would consider an individual to be a subject's legally authorized representative for research as long as that state or local law

provides a “reasonable basis” for allowing that individual to provide informed consent for the subject.

The IRB will evaluate both the consent process and the procedures for documenting informed consent to ensure that adequate informed consent is obtained from subjects. Only appropriately trained members of the study team can obtain informed consent for a clinical trial.

5.2 Definitions

Legally authorized representative (LAR): Federal (45 CFR § 46.102(c): An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

New York State: Per the Family Health Care Decisions Act (FHCDA), a person in the highest category on the following surrogate list who is available, willing and competent to make decisions for the incapable patient, and is identified when there is no health care agent:

1. A court-appointed guardian (per NYS Mental Health Law Article 81);
2. An individual designated as a representative/agent through a health care proxy that is appropriately executed. For a health care proxy to be effective, it must have been signed at a time when the subject had decision-making capacity. The subject’s wishes, if any, with regard to research as expressed in the health care proxy govern (e.g. prohibiting all research or permitting only research which may provide a direct benefit);
3. The spouse, if not legally separated from the patient, or the domestic partner;
4. A son or daughter eighteen years of age or older;
5. A parent;
6. A brother or sister eighteen years of age or older; or
7. A close friend (meaning a person eighteen (18) years of age or older who has maintained such regular contact with the subject as to be familiar with the subject’s activities, health and beliefs).

Legal guardian: A person appointed by a court of appropriate jurisdiction.

5.3 General Requirements

Investigators must obtain consent prior to entering a subject into a study and/or conducting any procedures required by the protocol, unless consent is waived by the IRB.

It is the PI’s responsibility to ensure that any team member who conducts a consent process and obtains consent from a potential subject is appropriately trained to perform this activity. The

person so delegated must be knowledgeable about the research to be conducted and the consenting process, and must be able to answer questions about the study.

Except as provided elsewhere in these Standard Operating Procedures:

1. Before involving a human subject in research, an investigator shall obtain the legally effective informed consent of the subject or the subject's LAR
2. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the LAR sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence
3. The information that is given to the subject or the LAR shall be in language understandable to the subject or the LAR
4. The prospective subject or the LAR must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information
5. Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension
6. Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or LAR's understanding of the reasons why one might or might not want to participate
7. No informed consent may include any exculpatory language through which the subject or the LAR is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

These informed consent requirements are not intended to preempt any applicable federal, state, or local laws (including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe) that have additional requirements for informed consent to be legally effective.

5.4 Informed Consent Process

Informed consent must be obtained under the following circumstances:

1. Informed consent may only be obtained from subjects who have the legal and mental capacity to give consent. For subjects without that capacity, consent must be obtained from a legal guardian or a legally authorized representative.
2. The informed consent process shall be sought under circumstances that provide the subject (or legally authorized representative) with sufficient opportunity to consider whether or not to participate.
3. The informed consent process shall be sought under circumstances that minimize the possibility of coercion or undue influence.
4. The informed consent information must be presented in language that is understandable to the subject (or legally authorized representative). To the extent possible, the language should be understandable by a person who is educated to 8th grade level and layman's terms shall be used in the description of the research.
5. For subjects whose native language is not English, informed consent must be obtained in a language that is understandable to the subject (or to the subject's legally authorized representative). In accordance with this policy, the IRB requires that informed consent conferences include a reliable interpreter when the prospective subject does not understand the language of the person who is obtaining consent.
   - ***See section 17.8 for additional policy governing inclusion of non-English speakers.***
6. The informed consent process may not include any exculpatory language through which the subject is made to waive, or appear to waive any of the subject's legal rights or through which the investigator, the sponsor, the University employees or agents are released from liability for negligence, or appear to be so released.
7. Although the PI may delegate the responsibility of obtaining consent from subjects to other members of his/her research team, the PI retains ultimate responsibility for insuring that each prospective subject is adequately informed about all aspects of the research and understands the information provided. It is the PI's responsibility to train and supervise the study personnel who are obtaining consent
8. The individual who signs the consent form as the 'person obtaining consent' is responsible for leading the potential subject through the entire consent process. This means:

    a. All aspects of the study, as described in the consent form, are first discussed with the potential subject;
    b. The consent form is thoroughly reviewed with the potential subject and answers to the potential subject's questions are provided;
    c. While reviewing the consent form, the person obtaining consent asks questions designed to assess the potential subject's understanding of the material. The person will specifically state this intent to the potential subject (i.e. the person is making sure the potential subject appreciates what s/he is being asked to do, and why);

d. The potential subject is given ample opportunity to decide, without coercion or undue influence, whether or not to be in the study; and
e. The consent process does not end with the formal signing of the consent document. Rather, it is an ongoing process that continues throughout the subject's participation in the study. The person obtaining consent remains responsible for continued assessments of the subject's understanding of what is happening to him/her, his/her willingness to participate and for providing the subject with any new information that may affect their willingness to participate.

5.5 Determining a potential adult subject's ability to consent to research

For the purpose of this section, a subject has the capacity to consent to his or her own participation in a research activity if s/he demonstrates the following:

1. That the activity is research, not standard treatment;
2. The risks and benefits of a study;
3. The alternatives that are available if s/he does not participate; and
4. The decision not to participate will be accepted without penalty, i.e. without jeopardizing clinical care.

In reaching a decision about participation, it is essential for the potential subject to demonstrate an ability to use this information in a rational manner. Thus, in considering risks, benefits, and available alternatives, subjects must show they understand the aspects of these factors that are unique to them as individuals. To highlight this distinction, a person who is suffering with severe depression may be able to demonstrate an appreciation of 1, 2, 3 and 4 above, but may not care, or may actually want to take risks. Such individuals should not be considered able to provide consent for themselves.

See Section 6.9 for further discussion regarding adults who cannot consent for themselves.

5.6 Basic Elements of Informed Consent

1. A statement that the **study involves research**, an explanation of the **purposes** of the **research** and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental; a description of any reasonably foreseeable **risks** or discomforts to the subject;
2. A description of any **benefits** to the subject or to others which may reasonably be expected from the research;
3. A disclosure of appropriate **alternative procedures** or courses of treatment, if any, that might be advantageous to the subject;

4. A statement describing the extent, if any, to which confidentiality of records identifying the subject must be maintained;
5. For research involving more than minimal risk, an explanation as to the availability of medical treatment in the case of **research-related injury**, including who will pay for the treatment and whether other financial compensation is available (see section 17.6 for SBU policy on Industry-funded clinical trials);
6. An explanation of whom to contact on the research team for answers to pertinent **questions about the research,** or to voice concerns or complaints about the research, and whom to contact in the event of a research-related injury to the subject and whether any medical treatment is available if injury occurs, what it consists of and where further information may be obtained;
7. Contact information for the IRB to obtain answers to questions about the research; to voice concerns or complaints about the research; to obtain answers to **questions about their rights as a research subject**; in the event the research staff could not be reached; and in the event the subject wishes to talk to someone other than the research staff for problems, concerns, information or input.
8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled;
9. One of the following statements about any research that involves the **collection of identifiable private information or identifiable biospecimens**:

    a. A statement that **identifiers might be removed** from the identifiable private information or identifiable biospecimens **and that**, after such removal, the information or biospecimens **could be used** for future research studies or distributed to another investigator for future research studies **without additional informed consent** from the subject or the legally authorized representative, if this might be a possibility; or

    b. A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, **will not be used or distributed** for future research studies.

For FDA-regulated studies, add the possibility that the Food and Drug Administration may inspect the records needs to be included in the statement regarding subject confidentiality.

For <u>applicable</u> clinical trials (see Section 17.4), the following statement must be included verbatim:

"A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

Additional elements of informed consent to be applied, as appropriate:

1. A statement that the particular treatment or procedure may involve risks to the subject, which are currently unforeseeable. (e.g. include when the research involves investigational test articles or other procedures in which the risks to subjects is not well known)
2. A statement that if the subject is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus, which are currently unforeseeable. (For example: Include when the research involves pregnant women or women of childbearing potential and the risk to fetuses of the drugs, devices, or other procedures involved in the research is not well known)
3. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent. (e.g. include when there are anticipated circumstances under which the investigator may terminate participation of a subject)
4. Any additional costs to the subject that may result from participation in the research. (e.g. include when it is anticipated that subjects may have additional costs)
5. The consequences of a subject's decision to withdraw from the research. (e.g. include when withdrawal from the research is associated with adverse consequences)
6. Procedures for orderly termination of participation by the subject. (e.g. include when the protocol describes such procedures)
7. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject. (e.g. include when the research is long term and interim information is likely to be developed during the conduct of the research)
8. The approximate number of subjects involved in the study. (e.g. include when the research involves more than minimal risk)
9. A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;
10. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions;
11. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).
12. The amount and schedule of all payments.

The consent process will be documented according to legal and regulatory requirements.

5.7 Documentation of Informed Consent

Except as provided in Section 5.12 of this document, informed consent must be documented by the use of a written consent form approved by the IRB.

1. Informed consent is documented by the use of a written consent form approved by the IRB and signed (including in an electronic format) and dated by the subject or the subject's legally authorized representative at the time of consent. For those consent forms that must be translated into a foreign language, an affidavit of accurate translation from the IRB approved English version must be provided from an appropriate translator who is unaffiliated with the study. The translated consent form and affidavit must be submitted and approved by the IRB before its use. The individual obtaining a non-English speaking subject's consent should either be a study investigator who is fluent in both languages, or a study investigator who is assisted by either a qualified interpreter or a recognized interpreter service. See section 17.8 for additional policy governing inclusion of non-English speakers.
2. For research conducted in accordance with ICH-GCP E6 or in facilities subject to Joint Commission requirements, the name of the person who obtained consent and the date they did so is documented on the written consent form;
3. A written copy of the signed and dated consent form must be given to the person signing the form. The investigator should retain the signed original in the research records. When appropriate, a copy of the consent form is uploaded into the electronic health record;
4. Documentation of consent must be either via:
   A written consent document embodies the basic and required additional elements of informed consent including required disclosures when the research involves private identifiable information or identifiable biospecimens. The investigator shall give either the subject or the subject's LAR adequate opportunity to read the informed consent form before it is signed; alternatively, this form may be read to the subject or the subject's legally authorized representative;
   or
   A short form written consent document which states that the elements of informed consent have been presented orally to the subject or the subject's legally authorized representative and the key information required above was presented first to the subject, including required disclosures when the research involves private identifiable information or identifiable biospecimens before other information, if any, was provided. When this method is used:

- There must be a witness to the oral presentation; and
- The IRB must approve a written summary of what is to be signed by the subject or representative; and
- The witness must sign both the short form and a copy of the summary; and
- The person actually obtaining consent must sign a copy of the summary; and

- A copy of the signed summary must be given to the subject or representative, in addition to a copy of the signed short form.

When this 'short form' procedure is used with subjects who do not speak English:

- The oral presentation and the short form written document should be in a language understandable to the subject;
- The IRB approved English language informed consent document may serve as the summary; and
- The witness should be fluent in both English and the language of the subject. When the person obtaining consent is assisted by an interpreter, the interpreter may serve as the witness, but must be unaffiliated with the study. The IRB must receive and approve all foreign language versions of the short form document (along with translator affidavit) prior to use.
- In addition to receiving a copy of the (English) summary and a copy of the short form at the time of consenting, the subject must receive a copy of the summary, translated into their native language, as soon as possible after their enrollment into the study.

Note: that English and Spanish versions of an IRB acceptable 'short form' document are available in the Forms Library within the electronic management system. Expedited review of these versions is acceptable if the protocol, the full English language informed consent document, and the English version of the short form document have already been approved by the convened IRB. **See section 17.8 for additional policy governing inclusion of non-English speakers.**

5.8 Special Consent Circumstances

5.8.1 Non-English Speaking Subjects

See section 17.8 for SBU policy on non-English speaking subjects

5.8.2 Consenting Subjects Who Read Braille

For blind subjects who read Braille, the IRB may approve a consent document prepared in Braille. In order to assure itself that a Braille consent document is accurate, the IRB may require a transcription into print text or review of the document by an IRB member or other person who reads Braille. If possible, the subject will sign the Braille consent; otherwise consent will be obtained, witnessed and documented as described below in section 5.8.4.

5.8.3 Consenting Subjects in American Sign Language (ASL)

For deaf subjects who are fluent in ASL, the IRB may approve a consent process using ASL and the IRB approved written consent form. When this process is approved, the individual authorized to consent the prospective subject must use an interpreter fluent in ASL to conduct the consent process and the documentation of the consent process must conform to the requirements set forth in section 5.7.

5.8.4 Consenting Subjects who are Blind or Illiterate

When subjects are unable to read a written consent form (such as blind or illiterate subjects), the IRB may approve an alternate form of the consent process, provided the subject (1) retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained verbally and (2) is able to indicate approval or disapproval to study entry.

In this process, the consent form must be read to the subjects and the subjects must be given an opportunity to ask questions. An audiotape approved by the IRB may be used. If capable of doing so, the subject signs, or marks an X to signify consent. If that is not possible, the subject will provide consent verbally. The person obtaining consent and a witness will sign the written study consent form with a statement that documents that an oral process was used and, if necessary, that the subject gave consent. The consent process will also be documented in the medical record or in accord with the Institution's policy. Signed copies of the consent form are given to the subject and, whenever possible, these documents may be provided to the subject on audio or video tape.

For research that is no more than minimal risk, documentation of consent may be waived if the criteria at Section 5.12 are met.

5.9 Consent Monitoring

The IRB has the authority under 45 CFR 46.109(e) and 21 CFR 56.109(f) to conduct special monitoring/observation the informed consent process for human research studies in order to protect the rights and welfare of research participants.

As part of the routine QA assessment program, the Office of Research Compliance notifies PI's, via the IRB approval letter, to contact the office when the first subject is scheduled to be consented. If scheduling permits, an ORC staff member will observe the consent process in order to:

- Assure that the research teams satisfy all federal, state and institutional requirements for obtaining consent from research participants;
- Assure that an appropriate consent process is followed, appropriately completed and documented;
- Assure the approved consent process is being followed;
- Assure the information provided to the participant was accurate and conveyed in understandable language;
- Assure the participant had sufficient time to consider study participation;
- Assure the possibility of coercion and undue influence are not evident;
- Ensure that subjects are truly giving Informed Consent; and
- Assure the subject appeared to understand the information and gave their voluntary consent.

The consent monitoring process can also be done via general, random not-for-cause reasons, or it may be determined by the IRB that such consent monitoring is warranted.

The factors that the IRB may consider in making the determination that special monitoring of the consent process may include, e.g.:

- High risk studies;
- Studies that involve complex and complicated procedures or interventions;
- Studies involving Vulnerable Populations (e.g., children, adults unable to consent for themselves);
- Studies involving study staff with minimal experience in administering consent to study participants;
- Concerns raised about study team performance, such as prior findings of noncompliance related to the consent process;
- Presence of study team conflicts of interest;
- Prior complaints about the consent process.

The consent monitoring may be conducted by IRB staff, IRB members or another party appointed by the IRB Chair. The PI will be notified of the pending consent monitoring process arrangements will be made with the PI for the monitoring of the consent process.

Following the monitoring, a report of the findings will be submitted to the IRB and reflected in the minutes. The Board can then take actions appropriate to the report (e.g., follow non-compliance procedure etc.). The PI will be notified by email regarding the outcome of the monitoring and any resulting IRB determinations (if any).

5.10 Subject Withdrawal or Termination

For a variety of reasons, a subject enrolled in a research study may decide to withdraw from the research, or an investigator may decide to terminate a subject's participation in research regardless of whether the subject wishes to continue participating. In these circumstances, questions sometimes arise about:

1. Whether the investigator may use, study, or analyze already collected data about the subject who withdraws from the research or whose participation is terminated by the investigator; And
2. Whether the investigator can continue to obtain data about the subject and if so, under what circumstances. The following addresses these and related questions. Investigators must plan for the possibility that subjects will withdraw from research and include a discussion of what withdrawal will mean and how it will be handled in their research protocols and informed consent documents.

Regulatory requirements regarding the retention and use of data after subject withdrawal or termination differ depending on whether or not the research is subject to FDA regulations.

When seeking informed consent from subjects, the following information regarding data retention and use must be included:

- For FDA-regulated clinical trials, when a subject withdraws from a study, the data collected on the subject to the point of withdrawal remain part of the study database and may not be removed. The consent document cannot give the subject the option of having data removed.
- For research not subject to FDA regulations, the investigator should inform subjects whether the investigator intends to either: (1) retain and analyze already collected data relating to the subject up to the time of subject withdrawal; or (2) honor a research subject's request that the investigator destroy the subject's data or that the investigator exclude the subject's data from any analysis.

Sometimes, a subject wants to withdraw from the primary interventional component of a study, but is willing to allow the investigator to continue other research activities described in the IRB-approved protocol and informed consent document that involve participation of the subject, such as:

- Obtaining data about the subject through interaction with the subject (e.g., through follow-up interviews, physical exams, blood tests, or radiographic imaging); or

- Obtaining identifiable private information from the subject's medical, educational, or social services agency records or from the subject's healthcare providers, teachers, or social worker.

When a subject's withdrawal request is limited to discontinuation of the primary interventional component of a research study, research activities involving other types of participation for which the subject previously gave consent may continue. The investigator should ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through noninvasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.

If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous paragraph, the investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). IRB approval of informed consent documents would be required.

If a subject a) withdraws from the interventional portion of a study, (b) does not consent to continued follow-up of associated clinical outcome information, and (c) does not request removal of their data, the investigator must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent. However, an investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.

5.11 Waiver or Alteration of Informed Consent

An IRB may waive the requirement to obtain informed consent, provided the IRB finds and documents that the below criteria are satisfied.

Likewise, an IRB may approve a consent procedure that omits some, or alters some or all, of the basic and additional elements of informed consent (an "alteration"), provided that the IRB finds and documents that the below criteria are satisfied.

1. The research or clinical investigation involves no more than minimal risk to the subjects;
2. The research or clinical investigation could not practicably be carried out without the requested waiver or alteration;

3. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format (This criterion is not included in FDA or DoJ/NIJ regulations);
4. The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
5. Whenever appropriate, the subjects or LARs will be provided with additional pertinent information after participation.

These criteria may be applied to research subject to FDA regulation as well (although criterion #3 is not required for an FDA determination)

Waivers/Alterations of consent in research Involving public benefit and services programs conducted by or subject to the approval of state or local officials

An IRB may waive the requirement to obtain informed consent, provided the IRB finds and documents that the below criteria are satisfied. Likewise, an IRB may approve a consent procedure that omits some, or alters some or all, of the basic and additional elements of informed consent (an "alteration"), provided that the IRB finds and documents that the below criteria are satisfied.

1. The research or demonstration project is to be conducted by, or is subject to the approval of, state or local government officials and is designed to study, evaluate, or otherwise examine:
   a. Public benefit or service programs;
   b. Procedures for obtaining benefits or services under those programs;
   c. Possible changes in or alternatives to those programs or procedures; or
   d. Possible changes in methods or levels of payment for benefits or services under those programs.
2. The research could not practicably be carried out without the waiver or alteration.

This option does NOT apply to FDA-regulated research.

Screening, recruiting, or determining eligibility

An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met:

1. The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or

2. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

The FDA does not consider records review or oral communication with the subject prior to obtaining consent to be part of the clinical investigation, therefore consent for these activities need not be obtained and waivers are not required.

5.12 Waiver of Documentation of Informed Consent

The IRB may waive the requirement for the investigator to obtain a signed consent form or signed parental permission form for some or all subjects if it finds any of the following:

1. Only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality; or

Note 1: *Subjects (or LARs) must be asked whether they want documentation linking them with the research, and their wishes must govern. (Example: domestic violence research where the primary risk is discovery by the abuser that the subject is talking to investigators.)*

Note 2: *In order to waive written documentation of consent where the only record linking the subject and the research would be the consent document, the IRB has to determine that the research is not FDA-regulated.*

Or

2. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. This option **does not** apply to FDA-regulated research.

3. If the subjects or LARs are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained. This option **does not** apply to FDA-regulated research.

In cases in which the documentation requirement is waived, the IRB requires the investigator to provide in the application materials a written summary of the information to be communicated to the subject. The summary will contain all require and appropriate additional elements of consent. The IRB will consider whether to require the investigator to provide subjects with a written statement regarding the research.

Unless the IRB has granted a full waiver of the requirement to obtain informed consent, investigators who seek and receive approval for a waiver of documentation of consent still must perform an appropriate consent process.

5.13 Waiver of Informed Consent for Planned Emergency Research

In accordance with 21 CFR 50.24, the IRB will consider for review and approval planned research involving life-threatening emergencies where a waiver is proposed for requirement to obtain prospective informed consent.

The conduct of planned research in life-threatening emergencies where the requirement to obtain prospective informed consent has been waived by the IRB is covered by 21 CFR §50.24 for FDA regulated research and by the waiver articulated by HHS at 61 FR 51531-33 for non-FDA regulated research. Among other requirements, the research plan must be carried out under an approved IND or IDE, if applicable, and must be approved in advance by the IRB, and publicly disclosed to the community in which the research will be conducted. The waiver of informed consent is not applicable to research involving children (subpart D), fetuses, pregnant women and human in vitro fertilization (subpart B) and research involving prisoners (subpart C).

Research that proceeds according to this pathway is subject to prospective IRB approval, as opposed to Emergency Use research approved pursuant to 21 CFR §56.104(c).

5.13.1 Planned Emergency Research

The FDA exception from informed consent requirements for emergency research under FDA regulations, *21 CFR 50.24,* permits planned research in an emergency setting when human subjects who are in need of emergency medical intervention cannot provide legally effective informed consent and the timing of the intervention is such that obtaining informed consent from legally authorized representatives (LARs) is not possible.

The Secretary of Health and Human Services (HHS) has implemented an Emergency Research Consent Waiver under *45 CFR 46.101(i)* with provisions identical to those of the FDA with the exception of the IND/IDE requirement and the definition of family member includes spouses of brother/sisters. The waiver is not applicable to research involving prisoners, see *45 CFR 46.101(i) & 46.306(b).*

An exception from consent in emergency medicine research supported by the Department of Defense (DoD) is prohibited unless the Secretary of Defense approves a waiver of the informed consent (provision of 10 USC 980).

Most planned emergency research involves the use of an FDA regulated test article and therefore is subject to FDA regulations as listed above. The IRB recommends PIs who are planning emergency research contact the ORC for assistance at least 4-5 months prior to the planned start date. The requirements are very complex and include consultation within the University, the community in which the research is to be conducted, the FDA, and the Department of Health and Human Services (DHHS).

These Emergency Research policies and procedures apply to Planned Emergency Research. Planned Emergency Research is different from Emergency Use of a Test Article as regulated under FDA *21 CFR 56.104(c).*

5.13.1.1 Definition

Planned Emergency Research: involves subjects who, because of their condition (e.g. unconsciousness) are in a life-threatening situation that makes intervention necessary, are unable to give informed consent, and to be effective, the intervention must need to be administered before obtaining informed consent from the subject's legally authorized representative is reasonably possible.

5.13.1.2 Policy/Procedures

The IRB committee that initially reviews and approves the planned emergency research may approve the study without requiring informed consent of all research subjects prior to initiating the research intervention if the IRB (that includes a member who is a licensed physician and who is not otherwise participating in the clinical trial) finds that the following criteria from FDA 21 CFR 50.24 have been met:

1. The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
2. Obtaining informed consent is not feasible because:
    a. The subjects will not be able to give their informed consent as a result of their medical condition;
    b. The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and
    c. There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
3. Participation in the research holds out the prospect of direct benefit to the subjects because:
    a. Subjects are facing a life-threatening situation that necessitates intervention;

   b. Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
   c. Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
4. The clinical investigation could not practicably be carried out without the waiver.
5. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.
6. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with 21 CFR 50.25 and 45 CFR 46.116 and 46.117. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with paragraph 7(e) of this section.
7. Additional protections of the rights and welfare of the subjects will be provided, including, at least:
   a. Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;
   b. Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;
   c. Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and investigators of the study, including the demographic characteristics of the research population, and its results;
   d. Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and
   e. If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the

clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

8. The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.
9. The IRB determinations required by this section and the documentation required by this section are to be retained by the IRB for at least three (3) years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with 21 CFR 56.115(b).
10. Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under 21 CFR 312.30 or 21 CFR 812.35.
11. If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under this section or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRBs that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

5.13.1.3 Community Consultation

Community Consultation is an extremely important requirement for conducting planned emergency research. The community in which the research is to take place and the persons that would likely be affected by the research must be informed and must agree that it is acceptable to begin the planned emergency research. Consultation with the community must be conducted prior to full approval by the IRB.

Depending on the nature of the research, community consultation may consist of any of the following activities:

- survey(s);
- questionnaire(s);
- focus groups; and
- Community meetings.

The content of these activities/meetings must be reviewed and agreed upon prior to conducting the consultations by the IRB Chair or designee and the IO or designee.

In order to facilitate educating, informing and publicly disclosing the plans for the investigation and its risks and expected benefits to the community in which the clinical investigation will be conducted, and from which the subjects will be drawn, every effort must be made to engage a representative sampling of persons or organizations in the affected community consultation process to obtain their input and agreement that the research should go forward. The IRB cannot approve Planned Emergency Research without this part of the process being completed in a thorough manner. All community meetings must include the Principal Investigator. A representative from the ORC, and where appropriate, a member of the IRB, may also attend. Upon completion of the community consultation process, the PI must present a written report to the IRB citing any and all issues raised through the process and conclusions. The IRB will determine if there is community support based on the report.

The PI is expected to keep and maintain detailed documentation that all of the above required procedures for planned emergency research and emergency waiver of consent are met. The documentation should be included in the submission to the IRB for full approval.

5.14 Posting of Clinical Trial Consent Forms

For each clinical trial conducted or supported by a Federal department or agency, one IRB approved informed consent form used to enroll subjects **must be posted by the awardee or the Federal department or agency component conducting the trial** on a publicly available Federal Web site (e.g., clinicaltrials.gov etc.) that will be established as a repository for such informed consent forms. (Clinical Trial Informed Consent Form Posting (45 CFR 46.116(h)))

Two publicly available federal websites that will satisfy the consent form posting requirement, as required by the revised Common Rule, have been identified: ClinicalTrials.gov and a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021). If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal Web site (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted or an exception to post the information.

The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

6 Vulnerable Subjects in Research

6.1 Policy

When some or all of the subjects in research conducted under the auspices of University are likely to be vulnerable to coercion or undue influence or have diminished decision-making capacity, the research must include additional safeguards to protect the rights and welfare of these subjects. This includes research reviewed through the expedite process. The IRB must ensure that all of the regulatory requirements for the protection of vulnerable subjects are met and that appropriate additional protections for vulnerable subjects are in place.

The following procedures describe the requirements for involving vulnerable subjects in research under the auspices of the University.

6.2 Definitions

Children: Persons who have not attained the legal age for consent to treatments or procedures involved in research, under applicable law of the jurisdiction in which the research will be conducted. Consistent with New York State Law, the IRB generally defines children as persons under eighteen years of age. For the purposes of these SOPs, children and minors both imply persons under eighteen years of age. NYS Public Health Law, at section 2504 speaks to who may consent (to medical care in general, but NY state law does not specifically reference who may consent to participation in research) as follows:

1. (Any person) 18 or older, or is the parent of a child or is married may give effective consent for medical, dental health and hospital services for himself or herself and the consent of no other person shall be necessary.

2. Any person who has been married or who has borne a child may give effective consent for medical, dental health and hospital services for his or her child.
3. Any person who is pregnant may give effective consent for medical, dental health and hospital services related to the pregnancy.

While consent by 'emancipated' individuals is not the general rule, there are other statutory provisions relating to consent for minors who are in military service or are seeking treatment for AIDS (PHL '2781) and other sexually transmitted diseases (PHL '2305).

In general, where the individual is a minor, the presumption is that he or she is not emancipated and the burden of proof rests on the individual asserting it. Because New York State law does not specifically address consent of children with majority status by virtue of "emancipation" with respect to research, the IRB will review issues of consent related to enrollment of these minor children in research on a case-by-case basis.

Children: (21 CFR 50.3) means persons who have not attained the legal age for consent to treatments or procedures involved in clinical investigations, under the applicable law of the jurisdiction in which the clinical investigation will be conducted

Children: (45 CFR 46.402) are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

Guardian: In New York, generally, the power of a guardian is dictated by the 'legally appointed guardian powers', which are determined in scope and duration by a court and described in the guardian papers. Guardian powers can be very limited (e.g. to financial matters only) or much broader. Prior to relying on guardian consent for a specific subject, a copy of the legal guardian papers must be sent to ORC who (in consultation with Counsel's office) will assess whether the scope and powers (if any exist at all) of the Guardian do or do not include the authority to consent to research. Obtaining guardian consent without first obtaining approval from ORC constitutes noncompliance with these SOPs.

Guardian: (45 CFR 46.402) An individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care

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

Fetus: Product of conception from the time of implantation until delivery.

Legally Authorized Representative: (21 CFR 50.3) means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's particpation in the procedure(s) involved in the research

Viable fetus: Now termed a "viable neonate."

Nonviable fetus: A fetus ex utero that, although living, is not able to survive to the point of independently maintaining heart and respiration. ***NOTE:*** *In 45 CFR 46 Subpart B, this definition is used as the definition of a non-viable neonate.*

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

In vitro fertilization: Any fertilization either of human ova, which occurs outside the body of a female, through a mixture of donor human sperm and ova or by any other means.

Federal (45 CFR § 46.102(c): An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

New York State: Per the Family Health Care Decisions Act (FHCDA), a person in the highest category on the following surrogate list who is available, willing and competent to make decisions for the incapable patient, and is identified when there is no health care agent:

1. A court-appointed guardian (per NYS Mental Health Law Article 81);
2. An individual designated as a representative/agent through a health care proxy that is appropriately executed. For a health care proxy to be effective, it must have been signed at a time when the subject had decision-making capacity. The subject's wishes, if any, with regard to research as expressed in the health care proxy govern (e.g., prohibiting all research or permitting only research which may provide a direct benefit);
3. The spouse, if not legally separated from the patient, or the domestic partner;
4. A son or daughter eighteen years of age or older;
5. A parent;
6. A brother or sister eighteen years of age or older; or
7. A close friend (meaning a person eighteen (18) years of age or older who has maintained such regular contact with the subject as to be familiar with the subject's activities, health and beliefs).

Neonate: Newborn.

Viable neonate: Being able, after delivery, to survive to the point of being independently maintaining heart and respiration (given the benefit of available medical therapy).

Non-viable neonate: Same as a non-viable fetus.

Pregnancy: The period of time from confirmation of implantation (through any of the presumptive signs of pregnancy, such as missed menses, or by a medically acceptable pregnancy test), until expulsion or extraction of the fetus.

Prisoner: An individual involuntarily confined or detained~~.~~. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

Surrogate Consent: Obtained from a legally authorized representative on behalf of a subject determined to lack decision-making capacity.

6.3 Involvement of Vulnerable Populations

When some or all of the subjects in a protocol are likely to be vulnerable to coercion or undue influence, the IRB should include additional safeguards to protect the rights and welfare of these subjects. Some of the vulnerable populations that might be involved in research include children, pregnant women, fetuses, neonates, prisoners, adults who lack the ability to consent, students, employees, or homeless persons.

If the IRB reviews research that targets for enrollment categories of subjects vulnerable to coercion or undue influence, the review process will include one or more individuals who are knowledgeable about or experienced in working with these subjects. For example, the IRB will include one or more individuals who are knowledgeable about or experienced in working with children, prisoners, or adults with limited decision-making capacity, when reviewing research that involves individuals from these populations.

6.4 FWA and the 45 CFR 46 Subparts

45 CFR 46 has additional subparts designed to provide extra protections for vulnerable populations that also have additional requirements for the IRB.

Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research

Subpart C - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects

Subpart D - Additional Protections for Children Involved as Subjects in Research

6.5 Procedures

Initial Review of Research Proposal:

1. The PI should identify the vulnerable subjects to be enrolled in the proposed research at initial review and provide the justification for their inclusion in the study.
2. The IRB evaluates the proposed plan for consent of the specific vulnerable populations involved. If the research involves adults unable to consent, the IRB evaluates the proposed plan for permission of legally authorized representatives.
3. The IRB evaluates and approves the proposed plan for the assent of subjects, if applicable.
4. The IRB evaluates the research to determine the need for additional protections.
5. The IRB assesses the adequacy of additional protections for vulnerable populations provided by the PI.

Continuing Review and Monitoring. At continuing review, the PI should identify the number of vulnerable subjects enrolled and any that needed an independent monitor in the progress report.

6.6 Research Involving Pregnant Women, Human Fetuses and Neonates

- The following applies to all research regardless of funding source. According to the University FWA, Subpart B of 45 CFR 46 applies only to DHHS funded research. The funding source-specific requirements are noted in the appropriate sections. Note that for Department of Defense-sponsored research, research involving pregnant women, is subject to DHHS Subpart B.
    - For purposes of applying Subpart B, the phrase “biomedical knowledge” must be replaced with “generalizable knowledge”
    - The applicability of Subpart B is limited to research involving pregnant women as participants in research that is more than minimal risk and includes interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as participants
    - Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g

6.6.1 Research Involving Pregnant Women or Fetuses

6.6.1.1 Research Not Funded by DHHS

Where the risk to the fetus is **no more than minimal**, no additional safeguards are required and there are no restrictions on the involvement of pregnant women in research.

Where the risk to the fetus is **more than minimal**, pregnant women or fetuses may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus;
3. Any risk is the least possible for achieving the objectives of the research;
4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent;
5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;
6. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. For children who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent;
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
10. Individuals engaged in the research will have no part in determining the viability of a neonate.

6.6.1.2 Research Funded by DHHS

For DHHS-funded research, 45 CFR Subpart B applies to all research involving pregnant women. Under 45 CFR Subpart B, pregnant women or fetuses may be involved in research funded by DHHS if all of the following conditions are met:

1. Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risk to pregnant women and fetuses.;
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
3. Any risk is the least possible for achieving the objectives of the research;
4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, then the consent of the pregnant woman is obtained in accord with the provisions for informed consent;
5. If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;
6. Each individual providing consent under paragraph 4 or 5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
7. For children who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent in Section 6.8.2;
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
10. Individuals engaged in the research will have no part in determining the viability of a neonate.

6.6.2 Research Involving Neonates of Uncertain Viability, and Nonviable Neonates

Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
2. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate;
3. Individuals engaged in the research will have no part in determining the viability of a neonate; and

4. The requirements of Neonates of Uncertain Viability or Nonviable Neonates (see below in this section) have been met as applicable.

Neonates of Uncertain Viability. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the following additional conditions have been met:

The IRB determines that:

1. The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or
2. The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
3. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with the provisions of permission and assent, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

Nonviable Neonates. After delivery, nonviable neonates may not be involved in research covered by this subpart unless the IRB determines that all of the following additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained;
2. The research will not terminate the heartbeat or respiration of the neonate;
3. There will be no added risk to the neonate resulting from the research;
4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
5. The legally effective informed consent of both parents of the neonate is obtained in accord with the provisions of permission and assent, except that the waiver and alteration of the provisions of permission and assent do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

Viable Neonates. A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of the IRB Review Process and Research Involving Children.

6.6.3 Research Involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material

Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, must be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.

If information associated with material described above in this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent sections of this manual are applicable.

6.6.4 Research Not Otherwise Approvable

6.6.4.1 Research Not Funded by DHHS

If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates, **and**, the research is not approvable under the above provisions, **then** the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research based on either:

1. That the research in fact satisfies the conditions of Section 6.6.2, as applicable; or
2. The following:
    a. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
    b. The research will be conducted in accord with sound ethical principles; and
    c. Informed consent will be obtained in accord with the provisions for informed consent and other applicable sections of this manual.

6.6.4.2 Research Funded by DHHS

DHHS funded research that falls in this category must be approved by the Secretary of Health and Human Services. If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare

of pregnant women, fetuses or neonates and the research is not approvable under the above provisions, then the research will be sent to OHRP for DHHS review.

6.7 Research Involving Prisoners

Prisoners are another of the three classes that are deemed so vulnerable to exploitation in research that there are special rules protecting them. In the past, prisoners were viewed as a convenient research population. They are housed in a single location, constitute a large and relatively stable population, and live a routine life. Unfortunately, all the things that make a prison and prisoners a convenient research population also allow for exploitation of prisoners.

The concern Subpart C and this policy based on Subpart C attempts to address is whether prisoners have any real choice in participation in research, or whether incarceration prohibits free choice.

The following applies to all research involving prisoners, regardless of funding source. The requirements in this section are consistent with Subpart C of 45 CFR 46, which applies to DHHS funded research.

Research involving a detainee as a human participant is prohibited.

- This prohibition does not apply to research involving investigational drugs and devices when the same products would be offered to US military personnel in the same location for the same condition.
- The exemption for research involving survey or interview procedures or observation of public behavior does not apply to research with children, except for research involving observations of public behavior when the researcher(s) do not participate in the activities being observed.

6.7.1 Applicability

This policy applies to all biomedical and behavioral research conducted under the auspices of the University involving prisoners as subjects. Even though the IRB may approve a research protocol involving prisoners as subjects according to this policy, investigators are still subject to the Administrative Regulations of the New York State Department of Corrections and any other applicable State or local law. [45 CFR 46.301]

Note that for Department of Defense sponsored research, research involving prisoners of war (POW) is prohibited. This includes any person captured, detained, held or otherwise under the control of DoD personnel (military and civilian, or contractor employee).

6.7.2 Minimal Risk

The definition of minimal risk in the Subpart C is different than in the rest of the federal regulations. According to 45 CFR 46.303, minimal risk is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

6.7.3 Composition of the IRB

[45 CFR 46.304]

In addition to satisfying the general requirements detailed in the IRB section of this manual, when reviewing research-involving prisoners, the IRB must also meet the following requirements:

- A majority of the IRB (exclusive of prisoner members) must have no association with the prison(s) involved, apart from their membership on the IRB.
- At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one the IRB, only one the IRB need satisfy this requirement.
- The prisoner representative is listed as an alternative member who becomes a voting member when needed
- At least one of the IRB committees will be duly constituted to review research involving prisoners. Consultation with ORC is strongly recommended if such research is proposed.

6.7.4 Review of Research Involving Prisoners

1. The prisoner representative must review research involving prisoners, focusing on the requirements in Subpart C. For research funded by the DoD, when the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum.
2. The prisoner representative must receive all review materials pertaining to the research (same as primary reviewer).
3. The prisoner representative must be present at a convened meeting when the research involving prisoners is reviewed. If the prisoner representative is not present, research involving prisoners cannot be reviewed or approved. The prisoner representative may attend the meeting by phone, video-conference, or webinar, as long as the representative is able to participate in the meeting as if they were present in person at the meeting.
4. The prisoner representative must present his/her review either orally or in writing at the convened meeting of the IRB when the research involving prisoners is reviewed.
5. Modifications.

a. Minor modifications to research may be reviewed using the expedited procedure described below, using either of the two procedures described based on the type of modification.
b. Modifications involving more than a minor change reviewed by the convened IRB must use the same procedures for initial review including the responsibility of the prisoner representative to review the modification and participate in the meeting (as described above).

6. Continuing review. Continuing review must use the same procedures for initial review including the responsibility of the prisoner representative to review the continuing review materials and participate in the meeting (as described above).
7. Expedited Review
   a. Research involving interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied. The prisoner representative must concur with the determination that the research involves no greater than minimal risk. The prisoner representative must review the research as a reviewer, designated by the chair, or consultant. This may be as the sole reviewer or in addition to another reviewer, as appropriate. Review of modifications and continuing review must use the same procedures for initial review using this expedited procedure including the responsibility of the prisoner representative.
   b. Research that does not involve interaction with prisoners (e.g. existing data, records review) may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied. Review by a prisoner representative is not required. The prisoner representative may review the research as a reviewer or consultant if designated by the IRB Chair. Review of modifications and continuing review must use the same procedures as initial review.

6.7.5 Incarceration of Enrolled Subjects

If a subject becomes a prisoner while enrolled in a research study that was not reviewed according to Subpart C and Subpart C applies, the IRB must:

1. Confirm that the subject meets the definition of a prisoner.
2. Terminate enrollment or review the research study under Subpart C if it is feasible for the subject to remain in the study.
3. Before terminating the enrollment of the incarcerated subject the IRB should consider the risks associated with terminating participation in the study. If the subject cannot be terminated for health or safety reasons, one of two options are available:
   a. Keep the subject enrolled in the study and review the research under Subpart C. If some of the requirements of Subpart C cannot be met, but it is in the best interests of the subject

to remain in the study, keep the subject enrolled and inform OHRP of the decision along with the justification; or
   b. Remove the subject from the study and keep the subject on the study intervention under an alternate mechanism such as compassionate use, off label use, etc.
4. If a subject is incarcerated temporarily while enrolled in a study:
   a. If the temporary incarceration has no effect on the study, keep the subject enrolled; or
   b. If the temporary incarceration has an effect on the study, handle according to the above guidance.

Otherwise, the IRB Chair shall require that all research interactions and interventions with the prisoner-subject (including obtaining identifiable private information) cease until the convened IRB can review this request to approve a change in the research protocol.

The convened IRB, upon receipt of notification that a previously enrolled human subject has become a prisoner, shall promptly re-review the research protocol to ensure that the rights and wellbeing of the human subject, now a prisoner, are not in jeopardy. The IRB should consult with a subject matter expert having the expertise of a prisoner representative if the IRB reviewing the research protocol does not have a prisoner representative.

If the prisoner-subject can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner-subject's confinement does not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research involving human subjects from continuing as approved, the convened IRB may approve a change in the study to allow this prisoner-subject to continue to participate in the research.

For Department of Defense (DoD) funded research, the following applies:

If a participant becomes a prisoner, and the researcher asserts to the IRB that it is in the best interest of the prisoner-participant to continue to participate in the research while a prisoner, the IRB Chair may determine that the prisoner-participant may continue to participate until the convened IRB can review this request to approve a change in the research protocol and until the organizational official and DoD Component office review the IRB's approval to change the research protocol.

Otherwise, the IRB Chair shall require that all research interactions and interventions with the prisoner-participant (including obtaining identifiable private information) cease until the convened IRB can review this request to approve a change in the research protocol. The convened IRB, upon receipt of notification that a previously enrolled human participant has become a prisoner, shall

promptly (no longer than 30 days) re-review the research protocol to ensure that the rights and wellbeing of the human participant, now a prisoner, are not in jeopardy.

The IRB should consult with a subject matter expert having the expertise of a prisoner representative if the IRB reviewing the research protocol does not have a prisoner representative. If the prisoner-participant can continue to consent to participate and is capable of meeting the research protocol requirements, the terms of the prisoner-participant's confinement do not inhibit the ethical conduct of the research, and there are no other significant issues preventing the research involving human participants from continuing as approved, the convened IRB may approve a change in the study to allow this prisoner-participant to continue to participate in the research. This approval is limited to the individual prisoner-participant and does not allow recruitment of prisoners as participants.

For Department of Justice (DoJ) funded research, the following applies:

For research conducted within the Bureau of Prisons, the researcher must assume responsibility for actions of any person engaged to participate in the research project as an associate, assistant, or subcontractor to the researcher.

When research is conducted within the Bureau of Prisons, the project must have an adequate research design and contribute to the advancement of knowledge about corrections.

For research conducted within the Bureau of Prisons:

Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.

- The selection of participants within any one organization must be equitable
- Incentives may not be offered to help persuade inmate participants to participate. However, soft drinks and snacks to be consumed at the test setting may be offered.
- Reasonable accommodations such as nominal monetary recompense for time and effort may be offered to non-confined research participants who are both:
    - No longer in Bureau of Prisons custody
    - Participating in authorized research being conducted by Bureau employees or contractors

For research conducted within the Bureau of Prisons, the organization, IRB, and researchers and research staff must follow the requirements of 28 CFR 512, including:

- The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing
- The research design must be compatible with both the operation of the prison facilities and protection of human participants. The researcher must observe the rules of the institution or office in which the research is conducted

- Any researcher who is a non-employee of the Bureau must sign a statement in which the researcher agrees to adhere to the provisions of 28 CFR 512
- All research proposals will be reviewed by the Bureau Research Review Board

For research conducted with the Bureau of Prisons:

- A non-employee of the Bureau may receive records in a form not individually identifiable when advance adequate written assurance that the record will be used solely as a statistical research or reporting record is provided to the agency
- Except as noted in the consent statement to the participant, the researcher must not provide research information that identifies a participant to any person without that participant's prior written consent to release the information. For example, research information identifiable to a particular individual cannot be admitted as evidence or used for any purpose in any action, suit, or other judicial, administrative, or legislative proceeding without the written consent of the individual to whom the data pertain.
- Except for computerized data records maintained at an official DoJ site, records that contain non-disclosable information directly traceable to a specific person may not be stored in, or introduced into, an electronic retrieval system
- If the researcher is conducting a study of special interest to the Office of Research and Evaluation (ORE) but the study is not a joint project involving ORE, the researcher may be asked to provide ORE with the computerized research data, not identifiable to individual participants, accompanied by detailed documentation. These arrangements must be negotiated prior to the beginning of the data collection phase of the project.

For research conducted within the Bureau of Prisons required elements of disclosure include:

- The identity of the researchers
- Anticipated uses of the results of the research
- The extent to which confidentiality of records identifying the participant will be maintained. For studies sponsored by the National Institute of Justice (NIJ), the participant should be informed that private, identifiable information will be kept confidential and will only be used for research and statistical purposes. If, due to sample size or some unique feature, the identity of the individual cannot be maintained, the participants need to be explicitly notified. If the researcher intends to disclose any information, the participant needs to be explicitly informed what information would be disclosed, under what circumstances, and to whom. The participant must be informed of any risks that might result from this disclosure and must explicitly provide written consent prior to participating in the research.
- A statement that participation is completely voluntary and that the participant may withdraw consent and end participation in the project at any time without penalty or prejudice (the inmate will be returned to regular assignment or activity by staff as soon as practicable)

- A statement regarding the confidentiality of the research information and exceptions to any guarantees of confidentiality required by federal or state law. For example, a researcher may not guarantee confidentiality when the participant indicates intent to commit future criminal conduct or harm himself or herself or someone else, or, if the participant is an inmate, indicates intent to leave the facility without authorization
- A statement that participation in the research project will have no effect on the inmate participant's release date or parole eligibility

For research conducted within the Bureau of Prisons, the researcher must have academic preparation or experience in the area of study of the proposed research.

- When submitting a research proposal, the applicant shall provide the following information:
  - A summary statement, which includes:
    - Names and current affiliations of the researchers.
    - Title of the study
    - Purpose of the study
    - Location of the study
    - Methods to be employed
    - Anticipated results
    - Duration of the study
    - Number of participants (staff or inmates) required and amount of time required from each
    - Indication of risk or discomfort involved as a result of participation
  - A comprehensive statement, which includes:
    - Review of related literature
    - Detailed description of the research method
    - Significance of anticipated results and their contribution to the advancement of knowledge
    - Specific resources required from the Bureau of Prisons
    - Description of all possible risks, discomforts, and benefits to individual participants or a class of participants, and a discussion of the likelihood that the risks and discomforts will actually occur
    - Description of steps taken to minimize any risks
- Description of physical or administrative procedures to be followed to:
  - Ensure the security of any individually identifiable data that are being collected for the study
  - Destruction of research records or removal of individual identifiers from those records when the research has been completed
- Description of any anticipated effects of the research study on organizational programs and operations

- Relevant research materials such as vitae, sample consent forms, questionnaires and interview schedules
- A statement regarding assurances and certification required by 28 CFR 46, if applicable

For National Institute of Justice funded research, a copy of all data must be de-identified and sent to the National Archive of Criminal Justice Data, including copies of the informed consent document, data collection instruments, surveys, or other relevant research materials.

- At least once a year, the researcher shall provide the Chief, Office of Research and Evaluation, with a report on the progress of the research
- At least 12 working days before any report of findings is to be released, the researcher shall distribute one copy of the report to each of the following: the chairperson of the Bureau Research Review Board, the regional director, and the warden of each institution that provided data or assistance. The researcher shall include an abstract in the report of findings
- In any publication of results, the researcher shall acknowledge the Bureau's participation in the research project
- The researcher shall expressly disclaim approval or endorsement of the published material as an expression of the policies or views of the Bureau
- Prior to submitting for publication the results of a research project conducted under this subpart, the researcher must provide two copies of the material, for informational purposes only, to the Chief, Office of Research and Evaluation, Central Office, Bureau of Prisons

6.7.6 Additional Duties of the IRB

[45 CFR 46.305]

In addition to all other responsibilities prescribed for IRB in the SBU Institutional Review Board and IRB Review Process sections of this manual, the IRB will review research involving prisoners and approve such research only if it finds that:

1. The research falls into one of the following permitted categories [45 CFR 46.306]:
    a. Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
    b. Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
    c. Research on conditions particularly affecting prisoners as a class (for example, research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults); or

d. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject.

2. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;
5. The information is presented in language which is understandable to the subject population;
6. Adequate assurance exists that parole Board will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and
7. Where the IRB finds there may be a need for follow-up examination or care of subjects after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing subjects of this fact.

6.7.7 Certification to DHHS (applies only to research conducted or supported by DHHS)

Under 45 CFR 46.305(c), the institution responsible for conducting research involving prisoners that is supported by HHS shall certify to the Secretary (through OHRP) that the IRB has made the seven findings required under 45 CFR 46.305(a). For all HHS conducted or supported research the University will send to OHRP a certification letter to this effect, which will also include the name and address of the institution and specifically identify the research protocol in question and any relevant HHS grant application or protocol. HHS conducted or supported research involving prisoners as subjects may not proceed until OHRP issues its approval in writing to the University on behalf of the Secretary under 45 CFR 46.306(a)(2). The Institutional Official will be the individual who will certify that the duties of the IRB have been fulfilled.

Under its authority at 45 CFR 46.115(b), OHRP requires that the institution responsible for the conduct of the proposed research also submit to OHRP a copy of the research proposal so that OHRP can determine whether the proposed research involves one of the categories of research

permissible under 45 CFR 46.306(a)(2), and if so, which one. The term "research proposal" includes the IRB approved protocol, any relevant HHS grant application or proposal, any IRB application forms required by the IRB, and any other information requested or required by the IRB to be considered during initial IRB review.

For DHHS-funded research, OHRP has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of its intent to approve such research.

For DHHS-funded research which require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after OHRP has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of its intent to approve such research.

The above requirement does not apply to research that is not HHS conducted or supported.

6.7.8 Waiver for Epidemiology Research

The Secretary of DHHS has waived the applicability of 45 CFR 46.305(a)(l) and 46.306(a)(2) for certain research conducted or supported by DHHS that involves epidemiologic studies that meet the following criteria:

1. In which the sole purposes are:
   - To describe the prevalence or incidence of a disease by identifying all cases, or
   - To study potential risk factor associations for a disease, and
2. Where the IRB has approved the research and fulfilled its duties under 45 CFR 46.305(a)(2)–(7) and determined and documented that:
   - The research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and
   - Prisoners are not a particular focus of the research.
3. The specific type of epidemiological research subject to the waiver involves no more than minimal risk and no more than inconvenience to the human subjects. The waiver would allow the conduct of minimal risk research that does not now fall within the categories set out in 45 CFR 46.306(a)(2).
4. The range of studies to which the waiver would apply includes epidemiological research related to chronic diseases, injuries, and environmental health. This type of research uses epidemiologic methods (such as interviews and collection of biologic specimens) that generally entail no more than minimal risk to the subjects.

5. In order for a study to be approved under this waiver, the IRB would need to ensure that, among other things, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of the data.

6.8 Research Involving Children

The following applies to all research involving children, regardless of funding source. The requirements in this section are consistent with Subpart D of 45 CFR 46, which applies to DHHS funded research and Subpart D of 21 CFR 50, which applies to FDA regulated research involving children.

6.8.1 Allowable Categories

Research on children must be reviewed and categorized by the IRB into one of the following groups (and if there is more than one possible study arm, a component analysis should be done to assess risk for each arm):

45 CFR 46.404; OHRP and if applicable, 21 CFR 50.51; FDA
Research not involving physical or emotional risk greater than that ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (i.e., **minimal risk**).

- Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 6.8.2.

45 CFR 46.405; OHRP, and if applicable 21 CFR 50.52; FDA
Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subject.

- The risk is justified by the anticipated benefit to the subjects;
- Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 6.8.2.

45 CFR 46.406; OHRP and if applicable 21 CFR 50.53; FDA
Research involving greater than minimal risk and no reasonable prospect of direct benefit to the individual subject, but likely to yield generalizable knowledge about the subject's disorder or condition.

- The risk represents a minor increase over minimal risk;
- The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
- Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 6.8.2.

Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children.

- Federally-funded research in this category must be approved by the Secretary of Health and Human Services.
- FDA-regulated research in this category must be approved by the Commissioner of Food and Drugs.
- For non-federally-funded, non-FDA research, the IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research based on either:
  - That the research in fact satisfies the conditions of the previous categories, as applicable; or
  - The following:
    - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
    - The research will be conducted in accord with sound ethical principles; and
    - Informed consent will be obtained in accord with the provisions for informed consent and other applicable sections of this manual.
- Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in Section 6.8.2.

6.8.2 Parental Permission and Assent

6.8.2.1 Parental Permission

The IRB must determine that adequate provisions have been made for soliciting the permission of each child's parents or guardians. The IRB may find that the permission of one parent is sufficient for research to be conducted under .404 & .405 above. IRB's determination of whether permission must be obtained from one or both parents will be documented in the electronic record when a protocol receives expedited review, and in meeting minutes when reviewed by the convened committee.

Consent from both parents is **required** for research to be conducted under .406 & 'Research not otherwise approvable' above unless:

1. One parent is deceased, unknown, incompetent, or not reasonably available; or
2. When only one parent has legal responsibility for the care and custody of the child.

The IRB may waive the requirement for obtaining permission from a parent or legal guardian if:

1. The research meets the provisions for a waiver; or

2. If the IRB determines that the research protocol is designed for conditions or a subject population for which parental or guardian permission is not a reasonable requirements to protect the subjects (e.g. neglected or abused children) provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

Permission from parents or legal guardians must be documented in accordance with and to the extent required by Section 5.7.

6.8.2.2 Assent from Children

Because **"assent"** means a child's affirmative agreement to participate in research, the child must actively show his or her willingness to participate in the research, rather than just complying with directions to participate and not resisting in any way. When judging whether children are capable of assent, as well as the assent process, the IRB is charged with taking into account nature of the proposed research activity, the ages, maturity, and psychological state of the children involved. The minor population to be studied may have a wide range of ability to provide assent. Some potential subjects may lack the cognitive or developmental ability to provide assent, regardless of chronologic age. Some children will have the capacity to assent, while others will not. In this situation, the IRB may require that the PI has a plan of assessing and documenting each child's capability of assenting, and of being able to comply with the study procedures. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is then no longer a necessary condition for proceeding with the research. Even when the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances detailed in the Waiver of Informed Consent section of this manual. IRB determinations regarding assent and the process to document assent are documented.

Each protocol is unique and is reviewed by the IRB accordingly. As such, the IRB's decision regarding assent (and documentation thereof) may necessarily vary from the general parameters below.

But, in general:

Assent will be required for:

1. Non-therapeutic protocols. Assent must be documented as follows:
   a. For 12-17 year olds: via an assent form (containing highly simplified 'consent' information--see section below about an “Assent Form") that the child signs; and
   b. For 7-11 year olds: a note in the subject's research record that the assent discussion has occurred and the child's agreement has been obtained.
2. Potentially therapeutic protocols (FDA-approved or investigational) where there are alternatives available outside of the research with similar risk/benefit profiles. Assent must be documented as follows:
   a. For 12-17 year olds: via an assent form (containing highly simplified 'consent' information—see section below about an Assent Form") that the child signs; and
   b. For 7-11 year olds: via a note in the subject's research record that the assent discussion has occurred and the child's agreement has been obtained.
3. Potentially therapeutic protocol involving FDA- approved drugs, devices, radiation, procedures, etc. used in an experimental way (dosages, scheduling, etc.). Assent must be documented as follows:
   a. For 12-17 year olds: via an assent form (containing highly simplified 'consent' information—see section below an “Assent Form") that the child signs.
   b. For 7-11 year olds: via a note in the subject's research record that the discussion has occurred and the child's agreement has been obtained.
4. Protocols that do not fit into categories (1), (2), or (3) above, but where assent is none-the-less required by NCI CIRB (for cooperative oncology protocols), or as otherwise required by the IRB. Assent must be documented as follows:
   a. For 7-11 year olds: via a note in the subject's research record that the discussion has occurred and the child's agreement has been obtained.

Assent is waived for:

1. Non-therapeutic protocols where results of biological tests are required in order to determine eligibility for potentially therapeutic protocols (certain COG protocols).
2. Potentially therapeutic protocols involving an experimental drug or procedure where there are no standard alternatives available, or where the risk/benefit profile of the standard alternatives that are available are such that participation in the protocol would be important to the health or well-being of the children.
3. Studies where the subject population is too young, or the capability of some or all of the children is so limited, that they cannot reasonably be consulted

Whether assent is required or waived, no physical or chemical means of restraint may be used on a minor subject unless specifically approved prior to use by the IRB.

6.8.2.2.1 Assent Form:

This document must be an accurate and complete, but highly simplified version of the approved consent form/permission form for the study. It must be understandable to a twelve (12) year old (approximately 7th grade).

Investigators should try to draft a form that is age appropriate and study specific, taking into account the typical child's experience and level of understanding, and composing a document that treats the child respectfully and conveys the essential information about the study. The assent form should:

1. Tell why the research is being conducted;
2. Describe what will happen and for how long or how often;
3. Say it's up to the child to participate and that it's okay to say no;
4. Explain if it will hurt and if so for how long and how often;
5. Say what the child's other choices are;
6. Describe any good things that might happen;
7. Say whether there is any compensation for participating; and
8. Who to ask for questions.

6.8.2.3 Children who are Wards ('Foster Children")

Children who are wards of the State or any other agency, institution, or entity must be specifically permitted by the IRB for inclusion in research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition. Such **research** must be:

1. Related to their status as wards; or
2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

If the research meets the condition(s) above, the IRB will require that an advocate must be appointed for each child who is a ward (one individual may serve as advocate for more than one child), in addition to any other individual acting on behalf of the child as legal guardian or in *loco parentis.*

The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research

and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

6.9 Persons with Impaired Decision-Making Capacity

The requirements in this section apply to all research involving adults with impaired decision-making capacity regardless of funding source. Section 5.5 should be reviewed for required processes to be followed to ascertain a subject's capacity to consent for research.

In order to include such a population in research, the investigator must demonstrate to the IRB that there is a compelling reason to do so, and that the aims of the research cannot be accomplished without their inclusion.

An appropriate legally authorized representative (LAR), as defined above, must give surrogate permission for the patient's inclusion in the research. The LAR must be told that their obligation is to try to determine what the subject would do if competent, or if the subject's wishes cannot be determined, what they think is in the incompetent person's best interest. The subject's assent should also be obtained whenever possible. If the subject's condition is such that decision-making capacity may be regained, the investigator is obligated to repeat the consent process with the subject, and obtain the subject's consent to continue in the study.

6.9.1 IRB Composition and Additional Protections

For research constituting more than minimal risk at least one IRB member who is knowledgeable about, or experienced in working with subjects who are decisionally-impaired, will be present for the review.

For research involving more than minimal risk, without the prospect of direct benefit to the subject, additional protections to the subjects may include one or both of the requirements below, as deemed appropriate by the IRB:

1. A documented determination by the IRB that the research is of **vital importance**, i.e., there is clear and significant evidence that the use of such a procedure or intervention presents a reasonable opportunity to further the understanding of the etiology, prevention, diagnosis, pathophysiology, or alleviation or treatment of a condition or disorder; and/or
2. Consultation with one or more representatives of a relevant advocacy group.

As with any study, the IRB retains the right to have a member of the IRB or ORC to monitor/witness the consent processes with the patient's LAR.

6.9.2 Determining Decision Making Capacity

(See Section 5.5 for general discussion of the consent process required to determine the decision-making capacity of all potential research subjects.)

1. Certain individuals, such as those with severe dementia, or severe mental retardation, will have a diminished capacity to provide consent. For these individuals, see the section on 'Surrogate Consent,' below.
2. For other individuals, it will not always be easy to predict whether capacity will be diminished given the following:

- Many individuals with psychiatric illnesses have the capacity to provide consent.
- Medical illnesses (e.g. cerebral insult) may be accompanied by an impaired capacity to consent.
- Upon learning of a serious diagnosis (e.g. cancer), psychological "shock" may temporarily impair a person's capacity to provide consent, although the illness does not affect decisional capacity in and of itself.
- Individuals who are intoxicated with alcohol or with drugs may be unable to consent to research until the intoxication resolves.

In assessing capacity, it is important to note that capacity is neither a constant nor an absolute. For example:

- Stroke victims may not have the capacity to consent to research immediately after the onset of stroke, but may develop capacity as recovery progresses.
- Patients in the early stages of Alzheimer's disease may initially have the capacity to consent to research, but as the disease progresses, may lose the ability to decide to continue or withdraw from that research.
- Patients with schizophrenia often experience acute psychotic episodes followed by periods of lucidity.
- Patients who learn they are terminally ill, often experience an initial short-lived period of emotional shock and denial which impairs their capacity to provide consent.

The requisite level of capacity will necessarily vary from study to study and will depend on:

- The complexity of the information being presented, and
- The relative risks and benefits of the study (deciding to participate in a blood drawing protocol is 'easier' than deciding to participate in an experimental drug trial).

Therefore, when developing a research proposal, the investigator must determine whether the study will include any subjects who may not have the capacity to consent to the research, either initially, or at some point during the course of the study. If some or all subjects may have a

diminished capacity to consent, the investigator must further determine if the potential impairment is temporary (e.g. 'shock' at the discovery of a medical diagnosis, intoxication), permanent (e.g. severe mental retardation), progressive (e.g. Alzheimer's dementia) or fluctuating (e.g. bipolar disorder).

For research protocols involving subjects who have fluctuating or limited decision-making capacity the IRB may ensure that investigators establish and maintain ongoing communication with involved caregivers. Periodic re-consent should be considered in some cases. Third party consent monitors may be used during the recruitment and consenting process, or waiting periods may be required to allow more time for the subject to consider the information that has been presented.

It is often possible for investigators and others to enable persons with some decisional impairments to make voluntary and informed decisions to consent or refuse participation in research. Potential measures include repetitive teaching, group sessions, audiovisual presentations, and oral or written recall tests. Other measures might include follow-up questions to assess subject understanding, videotaping or audio-taping of consent interviews, second opinions, use of independent consent observers, interpreter for hearing-impaired subjects, allowing a waiting period before enrollment, or involvement of a trusted family member or friend in the disclosure and decision making process.

Both investigators and IRB members must be aware that for some subjects, their decision-making capacity may fluctuate. For subjects with fluctuating decision making capacity or those with decreasing capacity to give consent, a re-consenting process with surrogate consent may be necessary.

In the event research subjects become incompetent or impaired in decision making capacity after enrollment, the PI is responsible for notifying the IRB and ORC. The PI is responsible for developing a monitoring plan which follows the guidelines outlined above for impaired decision making research subjects.

Depending on the study, associated risk/benefit ratio, and likelihood of inclusion of adults who can and cannot consent for themselves, the IRB may require investigators to use independent and qualified professionals (not associated with the study and with familiarity concerning capacity to consent issues) to assess whether potential subjects have the capacity to give voluntary, informed consent.

If the IRB requires such formal documentation of a subject's capacity, the following statement is added to the end of the consent form:

"My signature below attests to the fact that I am a licensed health care provider and I have interviewed (name of patient) on _____ (date). I have determined that s/he does_____ does not_____ have the capacity to consent to participation in this research activity, in that s/he is____ is not____ capable of appreciating a) that the activity described in this consent document constitutes research, not standard treatment, b) the risks and benefits of this study c) the alternatives that are available if s/he chooses not to participate, and d) that the decision to not participate will be accepted without penalty, i.e., without jeopardizing his/her clinical care."

Although unable to provide informed consent, some persons may resist participating in a research protocol for which permission has been given by their LAR. Under no circumstances may subjects be forced or coerced to participate.

When subjects lack the capacity to give consent, investigators may obtain permission from the legally authorized representative of a subject as described below.

A person who has been determined to lack capacity to consent to participate in a research study should be informed about the trial to the extent compatible with the subject's understanding and, if possible, the subject should give their assent to participate, sign and date the written informed consent or a separate assent form. If the person objects to participating, this objection should be heeded.

Where subjects lack the capacity to give consent, surrogate consent may be obtained from the subject's legally authorized/empowered representative (as defined in Section 5.2)**.**

7 FDA-Regulated Research

FDA regulations apply to research that involves a FDA-regulated *test article* in a *clinical investigation* involving *human subjects* as defined by the FDA regulations. For FDA-regulated research, the IRB must apply the FDA regulations at 21 CFR 50 and 21 CFR 56.-If the research is conducted or supported by a Common Rule agency or department, or if compliance with the Common Rule is required by state law or the terms of an award or contract, then the Common Rule must also be applied.
Clinical investigations of investigational drugs and biological products must be conducted according to FDA's IND regulations, 21 CFR Part 312, and other applicable FDA regulations. Evaluations of the safety or effectiveness of a medical device must be conducted according to FDA's IDE regulations, 21 CFR Part 812, and other applicable FDA regulations.

The following procedures describe the review of FDA-regulated research by the SBU IRB.

7.1 Definitions

Biologic: 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 technologies. In general, the term "drugs" includes therapeutic biological products.

Clinical Investigation: Any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical laboratory studies. [21 CFR 50.3(c)]

Dietary Supplement: A dietary supplement is a product taken by mouth that is intended to supplement the diet and that contains a dietary ingredient. The dietary ingredients in these products can include vitamins, minerals, herbs and other botanicals, amino acids, other dietary substances intended to supplement the diet, and concentrates, metabolites, constituents, extracts, or combinations of the preceding types of ingredients. [21 U.S.C. 321(ff)]

Emergency Use: The use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval. [21 CFR 56.102(d)]

Humanitarian Use Device (HUD): A medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year.

Investigational Drug: New drugs that have not yet been approved by the FDA or approved drugs that are being studied in a clinical investigation.

Investigational Device: A device (including a transitional device) that is the object of an investigation. Investigation, as it pertains to devices, means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device.

IND: An investigational new drug application in accordance with 21 CFR Part 312.

IDE: An investigational device exemption in accordance with 21 CFR 812.

In Vitro Diagnostic Product (IVD). Those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. [21 CFR 809.3(a)]

Non-Significant Risk (NSR) Device. An investigational device that does not meet the definition of a significant risk device.

Significant Risk (SR) Device. An investigational device that:

1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; or
2. Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; or
3. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
4. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. [21 CFR 812.3(m)]

7.2 FDA Exemptions

The following categories of clinical investigations are exempt from the requirements of FDA regulations for IRB review:

1. Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review. [21 CFR §56.104(c)]
2. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. [21 CFR §56.104(d)]

7.3 Clinical Investigations of Articles Regulated as Drugs or Devices

7.3.1 IND/IDE Requirements

For studies evaluating the safety or effectiveness of medical devices or experiments using drugs, biologics, dietary supplements, and other compounds that may be considered a drug or device under FDA regulations, the investigator must indicate on the IRB application whether an IDE or IND is in place, and, if not, the basis for why an IDE or IND is not needed. Documentation must be provided by the sponsor or the sponsor-investigator. Documentation of the IND/IDE could be a:

1. Industry sponsored study with IND/IDE number indicated on the protocol;
2. Letter/communication from FDA;
3. Letter/communication from industry sponsor; or
4. Other document and/or communication verifying the IND/IDE.

The investigator's brochure cannot be used to validate the IND or IDE. The Office of Research Compliance staff confirm that the test article has an IND or IDE or meets an exemption.

For investigational devices, the study may be exempt from IDE requirements (IDE-exempt) or, in the case of Non-significant Risk (NSR) device studies, follow abbreviated IDE requirements which do not require formal approval by the FDA. If a sponsor has identified a device study as IDE-exempt or NSR, then the investigator should include documentation with the submission providing the basis for IDE-exempt or NSR categorization for the IRB's consideration. If the FDA has determined that the study is IDE-exempt or NSR, documentation of that determination must be provided.

The IRB will review the application and, based upon the documentation provided, determine:

1. That there is an approved IND/IDE in place;
2. That the FDA has determined that an IND is not required or that a device study is IDE-exempt or NSR; or,
3. If neither of the above, whether an IND is necessary, or that a device study is exempt or NSR, or must be submitted to the FDA for an IDE or for a determination, using the criteria below.

The IRB cannot grant approval to the research until the IND/IDE status is determined, and, if necessary, an approved IND or IDE is in place. An IND goes into effect 30 days after the FDA receives the IND, unless the sponsor receives earlier notice from the FDA.

7.3.2 IND Exemptions

For drugs, an IND is not necessary if the research falls in one of the following seven (7) categories:

1. 21 CFR 312.2(b)(1): The drug being used in the research is lawfully marketed in the United States and all of the following requirements are met:
    a. The research is not intended to be reported to FDA as a well-controlled study in support of a new indication and there is no intent to use it to support any other significant change in the labeling of the drug;
    b. In the case of a prescription drug, the research is not intended to support a significant change in the advertising for the product;
    c. The research does not involve a route of administration, dose, subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
    d. The research is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively];
    e. The research is conducted in compliance with the requirements of 21 CFR 312.7 (i.e., the research is not intended to promote or commercialize the drug product); and
    f. The research does not intend to invoke FDA regulations for planned emergency research [21 CFR 50.24].

    NOTE: FDA has provided specific guidance for evaluating whether this exemption applies to studies of marketed drugs/biologics for the treatment of cancer.
2. 21 CFR 312.2(b)(2): For clinical investigations involving defined (blood grouping serum, reagent red blood cells, and anti-human globulin) in vitro diagnostic biological products, an IND is not necessary if a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and b) it is shipped in compliance with 312.160
3. 21 CFR 312.2(b)(5): A clinical investigation involving use of a placebo is exempt from the requirements of part 312 if the investigation does not otherwise require submission of an IND.
4. 21 CFR 320.31(b) and (d): Bioavailability or Bioequivalence (BA/BE) studies if all of the following conditions are met:
    a. The drug product does not contain a new chemical entity [21 CFR 314.108], is not radioactively labeled, and is not cytotoxic;
    b. The dose (single dose or total daily dose) does not exceed the dose specified in the labeling of the approved version of the drug product;

c. The investigation is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively]; and

d. The sponsor meets the requirements for retention of test article samples [21 CFR 320.31(d)(1)] and safety reporting [21 CFR 320.31(d)(3)].

5. 21 CFR 361.1: Research using a radioactive drug or biological product if all of the following conditions are met:

   a. It involves basic research not intended for immediate therapeutic, diagnostic, or similar purposes, or otherwise to determine the safety and efficacy of the product;

   b. The use in humans is approved by a Radioactive Drug Research Committee (RDRC) that is composed and approved by FDA;

   c. The dose to be administered is known not to cause any clinically detectable pharmacological effect in humans, and

   d. The total amount of radiation to be administered as part of the study is the smallest radiation dose practical to perform the study without jeopardizing the benefits of the study and is within specified limits.

6. FDA practices enforcement discretion for research using cold isotopes of unapproved drugs if all of the following conditions are met:

   a. The research is intended to obtain basic information regarding the metabolism (including kinetics, distribution, and localization) of a drug labeled with a cold isotope or regarding human physiology, pathophysiology, or biochemistry;

   b. The research is not intended for immediate therapeutic, diagnostic, or preventive benefit to the study subject;

   c. The dose to be administered is known not to cause any clinically detectable pharmacologic effect in humans based on clinical data from published literature or other valid human studies;

   d. The quality of the cold isotope meets relevant quality standards; and

   e. The investigation is conducted in compliance with the requirements for IRB review and informed consent. [21 CFR parts 56 and 50, respectively]

7.3.3 IDE Exemptions

For clinical investigations of medical devices, an IDE is not necessary if:

1. The research involves a device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time;
2. The research involves a device other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of 21 CFR 807 in determining substantial equivalence (a "510k" device);
3. The research involves a diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:
    a. Is noninvasive,
    b. Does not require an invasive sampling procedure that presents significant risk,
    c. Does not by design or intention introduce energy into a subject, and
    d. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure;
4. The research involves a device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk;
5. The research involves a device intended solely for veterinary use;
6. The research involves a device shipped solely for research on or with laboratory animals and labeled in accordance with 21 CFR 812.5(c);
7. The research involves a custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

7.3.4 Significant and Non-Significant Risk Device Studies

A device study is a Non-Significant Risk (NSR) Device study if it is not IDE exempt and does not meet the definition of a Significant Risk (SR) Device study.

Under 21 CFR 812.3(m), an SR device means an investigational device that:

1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
2. Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;

3. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
4. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

If the FDA has already determined a study to be SR or NSR, the FDA's determination is final and the IRB does not have to make the device risk determination.

Unless the FDA has already made a device risk determination for the study, the IRB will review studies that the sponsor or investigator have put forth as NSR at a convened meeting to determine if the device represents SR or NSR.

The sponsor or sponsor-investigator is responsible for providing the IRB with an explanation describing the basis for their initial determination of NSR and any other information that may help the IRB in evaluating the risk of the study (e.g., reports of prior investigations of the device).

The IRB will review the information provided by the sponsor and investigator including, but not limited to: the sponsor or investigator's NSR assessment, the description of the device, reports of prior investigations of the device (if applicable), the proposed investigational plan, and subject selection criteria.

The NSR/SR determination made by the IRB will be based on the proposed use of the device in the investigation, not on the device alone. The IRB will consider the nature of any harm that may result from use of the device, including potential harm from additional procedures subjects would need to undergo as part of the investigation (e.g., procedures for inserting, implanting, or deploying the device). The IRB may consult with the FDA or require the sponsor or investigator to obtain a determination from the FDA. The IRB will document the SR or NSR determination and the basis for it in the meeting minutes and provide the investigator, and sponsor when applicable, with the determination in writing.

Non-significant risk device studies do not require submission of an IDE application to the FDA but must be conducted in accordance with the abbreviated requirements of IDE regulations (21 CFR 812.2(b)). Under the abbreviated requirements, the following categories of investigation are considered to have approved applications for IDE's, unless FDA has notified a sponsor under 812.20(a) that approval of an application is required:

1. An investigation of a device other than a significant risk device, if the device is not a banned device and the sponsor (or sponsor-investigator):
    a. Labels the device in accordance with 812.5;

b. Obtains IRB approval of the investigation after presenting the reviewing IRB with an explanation of why the device is not a significant risk device, and maintains such approval;
c. Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under part 50 and documents it, unless the requirement is waived by the IRB;
d. Complies with the requirements of 812.46 with respect to monitoring investigations;
e. Maintains the records required under 812.140(b) (4) and (5) and makes the reports required under 812.150(b) (1) through (3) and (5) through (10);
f. Ensures that participating investigators maintain the records required by 812.140(a)(3)(i) and makes the reports required under 812.150(a) (1), (2), (5), and (7); and
g. Complies with the prohibitions in 812.7 against promotion and other practices.

When the FDA or IRB determines that a study is SR, the IRB may approve the study, but the study cannot begin until an IDE is obtained.

7.4 Diagnostic or Treatment Use of Humanitarian Use Devices

A Humanitarian Use Device (HUD) is an approved (marketed) medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 8,000 individuals in the United States per year [21 CFR 814.3(n)]. Federal law requires that an IRB approve the use of a HUD at a facility. Once approved, the clinical use of the HUD may be considered as any other approved device, with the caution that effectiveness has not been shown in clinical trials.

7.4.1 Definitions

Humanitarian Device Exemption: A "premarket approval application" submitted to FDA pursuant to Subpart A, 21 CFR Part 814 "seeking a humanitarian device exemption from the effectiveness requirements of sections 514 and 515 of the [FD&C Act] as authorized by section 520(m)(2) of the [FD&C Act]." HDE approval is based upon, among other criteria, a determination by FDA that the HUD will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from use of the device outweighs the risk of injury or illness from its use while taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

HDE Holder: A person or entity that obtains approval of an HDE from the FDA.

7.4.2 IRB Review Requirements

A Humanitarian Use Device (HUD) may only be used in a facility after an IRB has approved its use, except in certain emergencies. The HDE holder is responsible for ensuring that a HUD is provided only to facilities having an IRB constituted and acting in accordance with the FDA's regulations governing IRBs (21 CFR Part 56), including continuing review of use of the device.

When a HUD is used in a **clinical investigation** (i.e., research involving one or more subjects to determine the safety or effectiveness of the HUD), the full requirements for IRB review and informed consent apply (21 CFR 50 and 56) as well as other applicable regulations. It is essential to differentiate whether the HUD is being studied for the indication(s) in its approved labeling or for different indication(s). When the HUD is being studied for the indication(s) in its approved labeling, the IDE regulations at 21 CFR 812 do not apply. However, when the HUD is being studied for a different indication(s), 21 CFR 812 does apply, including the requirement for a FDA-approved IDE before starting the clinical investigation of a Significant Risk device.

7.4.3 Procedures

The relevant requirements and procedures for research described elsewhere in this manual apply to clinical investigations of HUDs. The material within this section applies to diagnostic or treatment uses of HUDs.

The health care provider seeking approval for diagnostic or treatment use of a HUD at SBU facilities is responsible for obtaining IRB approval prior to use of the HUD at the facility and for complying with the applicable regulations, including those for medical device reporting, organizational policies, and the requirements of the IRB.

Health care providers seeking initial IRB approval for diagnostic or treatment use of a HUD for the indication(s) in the HUDs approved labeling should submit the following materials to the IRB:

1. IRB Application Form;
2. A copy of the HDE approval letter from the FDA;
3. A description of the device, such as a device brochure;
4. The patient information packet for the HUD; and
5. The proposed clinical consent process

The IRB will review the proposal at a convened meeting ensuring that appropriate expertise is available either within the membership in attendance or via the use of consultants. The IRB will review the risks to patients that are described in the product labeling and other materials, the proposed procedures to ensure that risks are minimized, and will evaluate whether the risks are

reasonable in relation to the potential benefits to patients at the facility. The IRB will evaluate the patient information packet and proposed consent process and will determine if the materials are adequate and appropriate for the patient population.
The IRB may specify limitations on the use of the device, require additional screening and follow up procedures, require interim reports to the IRB, require continuing review more often than annually, or set other conditions or requirements as appropriate to minimize risks to patients and ensure the safe use of the device in the facility.

Once use of the HUD is approved, the health care provider is responsible for submitting any proposed changes to the IRB-approved plan or patient materials and obtaining approval for those changes prior to implementation, unless the change is necessary to avoid or mediate an apparent immediate risk to a patient. Proposed changes should be accompanied by any revised materials or supporting documentation. The IRB may review these changes using expedited review procedures or refer the changes for review by the convened IRB.

The health care provider is responsible for submitting reports to the FDA, the IRB, and the manufacturer/HDE Holder whenever a HUD may have caused or contributed to a death, and must submit reports to the manufacturer (or to FDA and the IRB if the manufacturer is unknown) whenever a HUD may have caused or contributed to a serious injury (21 CFR 803.30 and 814.126(a)). Serious injury means an injury or illness that (1) is life-threatening, (2) results in permanent impairment of a bodily function or permanent damage to a body structure, or (3) necessitates medical or surgical intervention to preclude permanent impairment of a bodily function or permanent damage to a body structure (21 CFR 803.3). The specific requirements for this reporting are in the Medical Device Reporting (MDR) Regulation, at 21 CFR Part 803. The IRB will review these reports via either expedited or convened review, as appropriate, and will consider whether any changes are needed to the IRB-approved plan or patient materials.

The health care provider is responsible for submitting continuing review materials to the IRB sufficiently in advance of the expiration date to ensure IRB review and re-approval prior to expiration. Materials to be submitted include:

1. The Continuing Review Application including information about each patient in which the device has been used;
2. The most recent periodic report to the FDA by the HDE holder and copies of safety information sent to the FDA, serious advers events or medical device reports;
3. The current patient information packet, if applicable;
4. The current consent, if applicable;
5. Any other new relevant information or materials or change in product labeling

The IRB may conduct continuing review using expedited review procedures or review by the convened IRB.

7.4.4 Emergency Use of HUDs

If an appropriately trained and licensed health care provider in an emergency situation determines that IRB approval for the use of the HUD at the facility cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be used without prior IRB approval. The health care provider must, within 5 days after the emergency use of the device, provide written notification of the use to the ORC including the identification of the patient involved, the date of the use, and the reason for the use. [21 CFR 812.124]

If a HUD is approved for use in a facility, but an appropriately trained and licensed health care provider wants to use the HUD outside its approved indication(s) in an emergency or determines that there is no alternative device for a patient's condition, the physician should consult with the HDE holder and IRB in advance if possible, obtain informed consent if possible, and ensure that reasonable measures are taken to protect the well-being of the patient such as a schedule and plan for follow up examinations and procedures to monitor the patient, taking into consideration the patient's specific needs and what is known about the risks and benefits of the device. The provider should submit a follow up report to the HDE holder and the IRB and must comply with medical device reporting requirements.

The IRB may require additional reports, patient protection measures, or other requirement, as appropriate given the specifics of the situation.

7.5 Expanded Access to Investigational Drugs, Biologics, and Devices

Expanded access pathways, are designed to make investigational medical products available as early in the drug and device evaluation process as possible to patients without therapeutic options, because they have exhausted or are not a good candidate for approved therapies and cannot enter a clinical trial. Expanded access refers to the use of investigational or unapproved/uncleared medical products (all referred to as "investigational" throughout this section) outside of a clinical trial, where the primary intent is treatment, rather than research. Because the products have not yet been approved by FDA as safe and effective, it is important to remember that the product may not be effective and there may be unexpected serious adverse effects and to take appropriate measures to ensure that this is understood by the patient or their LAR and to monitor for safety.

Charging for expanded access use of investigational products is discussed in Section 7.6.

7.5.1 Expanded Access to Investigational Drugs and Biologics

The FDA's expanded access rule for investigational drugs, including biologics classified as drugs, is intended to improve access to investigational drugs for patients with serious or immediately life-threatening diseases or conditions who lack other therapeutic options and may benefit from the investigational agent. Expanded access is sometimes referred to as compassionate use or treatment use.

For the purposes of expanded access to investigational drugs, ***immediately life-threatening disease or condition*** means a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. ***Serious disease or condition*** means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. [21 CFR 312.300(b)]

Expanded access may also apply to (1) situations when a drug has been withdrawn for safety reasons, but there exists a patient population for whom the benefits of the withdrawn drug continue to outweigh the risks; (2) use of a similar, but unapproved drug (e.g., foreign-approved drug product) to provide treatment during a drug shortage; (3) use of an approved drug where availability is limited by a risk evaluation and mitigation strategy (REMS); and (4) use for other reasons. All are referred to as "investigational" for the purposes of these SOPs.

Under the FDA's expanded access rule, access to investigational drugs for treatment purposes is available to:

- Individual patients, including an emergency [21 CFR 312.310]
- Intermediate-size patient populations [21 CFR 312.315]
- Widespread use under a treatment protocol or treatment IND [21 CFR 312.320]

The following section addresses expanded access for individual patients. Investigators seeking expanded access for intermediate-size populations or widespread use should consult with the ORC. Convened IRB review is generally required for intermediate or widespread expanded access unless the FDA has issued a waiver.
Physicians seeking access to investigational drugs under expanded access should work closely with the sponsor or manufacturer, the FDA, and the ORC, to determine the appropriate access mechanism and ensure that proper regulatory procedures are followed. The FDA provides

information about the procedures and requirements for expanded access on their website, including a link to the FDA's contact information.

7.5.1.1 Expanded Access to Investigational Drugs for Individual Patients

Expanded access to investigational drugs may be sought under an "Access Protocol" or an "Access IND". FDA generally encourages Access Protocols, which are managed and submitted by the sponsor of an existing IND, because it facilitates the review of safety and other information. However, Access INDs for the treatment of individual patients are also available and commonly used when: (1) a sponsor holding an existing IND declines to be the sponsor for the individual patient use (e.g., because they prefer that the physician take on the role of sponsor-investigator); or (2) there is no existing IND.

Sponsor or Manufacturer Approval:

Prior to submitting to the FDA or IRB, physicians seeking expanded access to an investigational drug should contact the sponsor (e.g., for investigational drugs under a commercial IND) or manufacturer (e.g., for approved drugs under a REMS) to: (1) ensure that the investigational drug can be obtained; (2) determine whether the patient may be treated under an existing IND study, sponsor-held Access Protocol, or if the physician should seek an Access IND; and (3) determine if the drug will be provided free or if there will be a charge. A Letter of Authorization (LOA) from the sponsor or manufacturer should be obtained.

FDA Approval:

When a commercial sponsor agrees to provide access under an Access Protocol, the sponsor is responsible for managing and obtaining FDA approval and all other sponsor responsibilities. A licensed physician under whose immediate direction an investigational drug is administered or dispensed for expanded access is considered an "investigator" under FDA regulations and is responsible for all investigator responsibilities under 21 CFR 312, to the extent they are applicable to expanded access.

If the sponsor or manufacturer declines treatment of the patient under an existing IND study or Access Protocol but agrees to make the investigational drug available for the patient, physicians may apply to the FDA for an individual patient Access IND using Form FDA 3926, a streamlined IND application specifically designed for such requests. Form FDA 3926, and related guidance, is available on a FDA website. Form FDA 3926 includes a section where an investigator can request approval from the FDA for alternative IRB review procedures; these alternative procedures enable review by the IRB Chair (or a Chair-designated IRB member) in lieu of review by the convened IRB.

This alternative review procedure is referred to as a "concurrence review" in FDA guidance; however, the IRB Chair must review the same materials and make the same determinations as the convened board would. The IRB Chair review can also be used for any post-approval reviews (e.g., unanticipated problems, continuing review, closure, etc.).

When there is an emergency situation and insufficient time to submit a written application to the FDA prior to treatment, a request to FDA for emergency use may be made by telephone (or other rapid means). A written expanded access application must be submitted within 15 days of the FDA's authorization.

A physician who obtains an Access IND is considered a "sponsor-investigator" and is responsible for the responsibilities of both sponsors and investigators under 21 CFR 312, as applicable, including IND safety reports, annual reports, and maintenance of adequate drug accountability records.

IRB Review:

Unless the conditions that permit an emergency use exemption are satisfied, IRB approval must be obtained prior to initiating treatment with the investigational drug. When the FDA has authorized the use of alternative IRB review procedures (which can be presumed when the request is made on Form FDA 3926 unless the FDA specifically states that the request is denied), the review may be conducted by the IRB Chair (or designee). Otherwise, the review must be conducted by the convened IRB.

Physicians using investigational drugs under compassionate use should develop and submit an appropriate plan and schedule for treating and monitoring the patient, taking into consideration the nature of the drug and the needs of the patient. The plan should include monitoring to detect any possible problems arising from the use of the drug.

To request IRB approval for single patient expanded access, investigators should contact the ORC and submit the following via the IRB electronic management system:

1. A complete patient history justifying the use, and details concerning the plan for treating and monitoring the patient;
2. A copy of the letter of authorization (LOA) from the Commercial Sponsor or Manufacturer or other documentation supporting sponsor/manufacturer approval;
3. A copy of the information submitted to the FDA (and FDA approval, if available);
4. A copy of the Investigator's Brochure or similar documentation that provides information regarding the potential risks and benefits of the investigational drug;

5. A copy of the draft informed consent document.

The IRB may review the expanded access application prior to FDA approval being received but cannot finalize approval until documentation of FDA approval is provided. The IRB will provide the investigator with written documentation of its review.

Post-Approval Requirements

Investigators are responsible for complying with any sponsor or FDA reporting requirements. The post-approval requirements for research described throughout this manual apply, including, but not limited to, prospective IRB approval of any proposed modifications to the plan or materials approved by the IRB unless the change is necessary to eliminate apparent immediate hazard to the subject (in which case it must be promptly reported), reporting of unanticipated problems, noncompliance, complaints, and other reportable information, and for continuing review and study closure, as applicable. **Additionally**, copies of any follow-up submissions to the FDA related to the expanded access use must be submitted to the IRB within 7 business days of the date of submission to the FDA.

Other reportable Information:

1. Notice of:
    a. Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated (classification as "OAI" is typically made after FDA has had the opportunity to review the responses to a 483), FDA Restrictions Placed on IRBs or Investigators, and any corresponding compliance actions taken under non-US authorities related to human research protections.
    b. Any litigation, arbitration, or settlements initiated related to human research protections.
    c. Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding human subject research conducted at or by SBU or SBU's program for the protection of human research participants.

NOTE: The above events (4.a, b, and/or c) must be reported to the ORC by phone and email as soon as anyone becomes aware, with the formal submission within the 7-day timeline as noted aboveEmergency Use of Investigational Drugs

FDA regulations permit the use of an investigational drug without IRB approval when an appropriately trained and licensed health care provider determines that IRB approval for the use of the drug cannot be obtained in time to prevent serious harm or death to a patient. The

provider is expected to assess the potential for benefit from the use of the drug and to have substantial reason to believe that benefits will exist.

Approval from the FDA and the Sponsor/Manufacturer must be obtained prior to initiating treatment with the drug.

Providers invoking the emergency use exemption must comply with any applicable FDA follow-up requirements including submission of safety reports, amendments, a summary following completion of treatment, and annual reports.

A copy of reports or amendments submitted to the FDA and any related correspondence must be submitted to the ORC.

Note: DHHS regulations do not permit research activities to be started, even in an emergency, without prior IRB approval. When emergency medical care is initiated without prior IRB review and approval, the patient may not be considered a research subject under 45 CFR Part 46.

DHHS regulations do not permit data obtained from patients to be classified as research involving human participants, nor permit the outcome of such care to be included in any report of a research activity subject to DHHS regulations.

The emergency use of a test article, other than a medical device, is however considered to be a clinical investigation, the patient is a participant, and the FDA may require data from an emergency use to be reported in a marketing application.

However, nothing in the DHHS regulations at 45 CFR Part 46 is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state or local law.

Emergency Use Exemption from Prospective IRB Approval

Under FDA regulations at 21 CFR 56.104(c), FDA exempts the emergency use of an investigational drug (or biologic classified as a drug) from the requirement for prospective IRB approval, provided that the conditions described below are satisfied and that the emergency use is reported to the IRB within 5 working days. Any subsequent use of the investigational drug in the facility requires IRB approval. However, FDA acknowledges that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue. If it appears likely that the investigational drug may need

to be used again, the IRB may request that a study application is submitted which would cover future uses.

FDA defines emergency use as the use of a test article

- **in a life-threatening* situation**
- **in which no standard acceptable treatment is available, and**
- **in which there is not sufficient time to obtain IRB approval** [21 CFR 56.102(d)].

If all conditions described in 21 CFR 56.102(d) exist, then the emergency exemption from prospective IRB approval found at 21 CFR 56.104(c) may be used.

***Life-threatening**, for the purposes of 21 CFR 56.102(d), includes both life-threatening and severely debilitating.

- **Life-threatening** means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.
- **Severely debilitating** means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

Unless the provisions for an emergency exception from the informed consent requirement are satisfied (see below), informed consent must be obtained in accordance with 21 CFR 50 and documented in writing in accordance with 21 CFR 50.27.

The IRB must be notified within **5 working days** after an emergency exemption is used via the IRB electronic management system. Notification must include justification that conditions a, b, and c above were met, as well as confirmation from the department chair concurring with the use and justification.

The IRB Chair will review the report to verify that circumstances of the emergency use conformed to FDA regulations. This must not be construed as IRB approval, as an exemption from the requirement for prospective IRB approval has been invoked. When appropriate, in the event a manufacturer requires documentation from the IRB prior to the emergency use, the IRB Chair or designee will review the proposed use, and, if appropriate, provide a written statement that the IRB is aware of the proposed use and considers the use to meet the requirements of 21 CFR 56.104(c). Reports of emergency use will be brought to the convened IRB for their information.

Investigators are reminded that they must comply with all other organizational policies and requirements applicable to the use of the investigational or unapproved drugs.

Emergency Exception from the Informed Consent Requirement

An exception under FDA regulations at 21 CFR 50.23(a-c) permits the emergency use of an investigational drug without informed consent when the investigator and an independent physician who is not otherwise participating in the clinical investigation (the emergency use) certify in writing all four of the following conditions:

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

If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject, and time is not sufficient to obtain the independent physician determination in advance of using the test article, the determinations of the clinical investigator shall be made and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

The IRB must be notified within **5 working days** when an emergency consent exception is invoked via the IRB electronic management system. Notification must include justification that the conditions above are met, as well as department chair concurrence. The IRB Chair will review the report to verify that circumstances of the emergency exception conformed to FDA regulations.

7.5.2 Expanded Access to Investigational and Unapproved Medical Devices

As with investigational drugs, unapproved medical devices may normally only be used in humans in an approved clinical trial under the supervision of a participating clinical investigator. However, there are circumstances under which a health care provider may use an unapproved device outside of a clinical study when it is not possible to enroll a patient in a clinical study and the patient is facing life-threatening circumstances or suffering from a serious disease or condition for which no other alternative therapy or diagnostic exists or is a satisfactory option for the patient.

FDA has made the following mechanisms available for these circumstances:

- Emergency Use
- Compassionate Use (or Single Patient/Small Group Access)
- Treatment Use

Investigators seeking access to investigational or unapproved devices under one of the above provisions should work closely with the sponsor or manufacturer, the FDA, and the ORC, to ensure that proper regulatory procedures are followed.

FDA has made information about expanded access to medical devices available on the FDA website.

7.5.3 Compassionate Use of Investigational/Unapproved Medical Devices

The compassionate use provision under expanded access provides a mechanism for accessing investigational devices for an individual patient or small groups of patients when the treating physician believes the device may provide a diagnostic or treatment benefit. Compassionate use can be used for devices being studied in a clinical trial under an IDE for patients who do not qualify for inclusion in the trial, and for devices for which an IDE does not exist. The following criteria must be satisfied:

1. The patient has a life-threatening or serious disease or condition; and
2. No generally acceptable alternative treatment for the condition exists.

The medical device company must agree to make the medical device available for the proposed compassionate use. FDA and IRB approval are required before the device may be used under the compassionate use provision.

FDA Approval:

When **there is an IDE** for the device, the IDE sponsor submits an IDE supplement requesting approval for the compassionate use under 21 CFR 812.35(a).

When **there is not an IDE** for the device, the physician or manufacturer submits the following information to the FDA:

1. A description of the device (provided by the manufacturer);
2. Authorization from the device manufacturer for the use;
3. A description of the patient's condition and the circumstances necessitating treatment or diagnostics (when seeking small group access, the number of patients to be treated;

4. A discussion of why alternative therapies/diagnostics are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition; and
5. The patient protection measures that will be followed, including:
    a. A draft of the informed consent document that will be used;
    b. Clearance from the institution as specified by their policies (see below);
    c. Concurrence (approval) of the IRB Chair or Chair-designated IRB member (prior to FDA request when possible); and
    d. An independent assessment from an uninvolved physician.

When IRB Chair approval cannot be obtained in advance of the submission to the FDA, the request should indicate that approval from the IRB Chair will be obtained prior to use of the device. Proof of IRB Chair approval must be submitted with the follow-up report to the FDA after the patient is treated (or the diagnostic is used).

When the compassionate use is conducted under an IDE, a licensed provider who receives an investigational device is an "investigator" under FDA regulations and is responsible and accountable for all applicable investigator responsibilities under 21 CFR 812 (IDE regulations), 21 CFR 50 (Informed Consent), and 21 CFR 56 (IRB).

When the provider obtains an IDE for compassionate use, the provider is considered a "sponsor-investigator" and is responsible for the responsibilities of both sponsors and investigators under 21 CFR 812, as applicable, including medical device reports and progress reports .

IRB Review:

Unless the conditions that permit an emergency use exemption are satisfied, IRB approval must be obtained prior to initiating treatment with the investigational device. When the request is for single-patient compassionate use, the review may be conducted by the IRB Chair (or designee). Otherwise, the review must be conducted by the convened IRB.

Physicians using medical devices under compassionate use should develop and submit an appropriate plan and schedule for treating and monitoring the patient, taking into consideration the nature of the device and the needs of the patient. The plan should include monitoring to detect any possible problems arising from the use of the device.

Standard submission procedures for initial approval of research should be followed. The following should be included, via the electronic management system:

1. A copy of the information submitted to the FDA (and FDA approval, if available);
2. A copy of the device brochure, Instructions for Use, or other similar documentation that provides information regarding the potential risks and benefits of the device;
3. A copy of the plan for treating and monitoring the patient; and
4. A copy of the draft informed consent document.

The IRB may review the expanded access application prior to FDA approval being received but may condition approval upon receipt of FDA approval. The IRB will provide the investigator with written documentation of its review.

Post-Approval Requirements

Investigators are responsible for complying with any sponsor or FDA reporting requirements. The post-approval requirements for research described throughout this manual apply, including, but not limited to, prospective IRB approval of any proposed modifications to the plan or materials approved by the IRB unless the change is necessary to eliminate apparent immediate hazard to the subject (in which case it must be promptly reported), reporting of unanticipated problems, noncompliance, complaints, and other reportable information, and for continuing review and study closure, as applicable. **Additionally**, a follow-up report to the FDA is required following a compassionate use by whomever submitted the original request to the FDA. The report should include summary information regarding patient outcome and any problems that occurred as a result of the device. A copy of the follow-up report to the FDA and any other post-approval submissions or reports to the FDA must be submitted to the IRB within 7 business days of the date of submission to the FDA.

Treatment Use of Investigational/Unapproved Medical Devices

During the course of a clinical trial under an IDE, if the data suggest that the device under study is effective, the trial may be expanded to include additional patients with life-threatening or serious diseases under the Treatment Use provision for expanded access. "Treatment Use" also applies to the use of a device for diagnostic purposes under these same conditions. [21 CFR 812.36]

The following criteria must be satisfied for Treatment Use to apply:

1. The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition;
2. There is no comparable or satisfactory alternative device available to treat or diagnose the disease or condition in the intended patient population;

3. The device is under investigation in a controlled clinical trial for the same use under an approved IDE, or all clinical trials have been completed; and
4. The sponsor of the controlled clinical trial is pursuing marketing approval/clearance of the investigational device with due diligence.

The IDE sponsor is responsible for applying for a Treatment Use IDE.

A licensed provider who receives an investigational device for treatment use under a Treatment Use IDE is an "investigator" under FDA regulations and is responsible and accountable for all applicable investigator responsibilities under 21 CFR 812 (IDE regulations), 21 CFR 50 (Informed Consent), and 21 CFR 56 (IRB).

IRB Review:

IRB approval is required before the investigational device/diagnostic is used. Standard submission procedures for approval of initial research should be followed.

Post-Approval Requirements

Investigators are responsible for complying with any sponsor or FDA reporting requirements. The post-approval requirements for research described throughout this manual apply, including, but not limited to, prospective IRB approval of any proposed modifications to the plan or materials approved by the IRB unless the change is necessary to eliminate apparent immediate hazard to the subject (in which case it must be promptly reported), for reporting of unanticipated problems, noncompliance, complaints, and other reportable information, and for continuing review and study closure, as applicable. **Additionally**, the semi-annual (applicable until the marketing application is filed) or annual (applicable after the marketing application is filed) progress report from the sponsor must be submitted to the IRB within 7 business days of receipt.

Emergency Use of Investigational Devices

FDA regulations permit the emergency use of an investigational or unapproved device without prior approval by the FDA or IRB when an appropriately trained and licensed health care provider determines that:

- The patient has a life-threatening or serious disease or condition that needs immediate treatment;
- No generally acceptable alternative treatment for the condition exists; and
- Because of the immediate need to use the device, there is no time to use existing procedures to obtain FDA approval for the use.

FDA expects the provider to make the determination that the above criteria are satisfied, to assess the potential for benefit from the use of the unapproved device, and to have substantial reason to believe that benefits will exist. Because prior FDA approval is not required, FDA expects providers planning the emergency use of an investigational device to obtain as many of the following as possible:

- An independent assessment from an uninvolved physician;
- Authorization from the device manufacturer;
- Concurrence of the IRB Chair or designee;
- Institutional clearance; and
- Informed consent from the patient or legally authorized representative.

At SBU, providers planning the emergency use of an investigational or unapproved device must contact the ORC as early in the process as possible and submit the justification for the use and above assessment/concurrence/clearances for review by the IRB Chair or designee. The IRB Chair or designee will review the information provided and determine whether the use conforms with FDA's requirements and expectations and whether the provisions for the protection of the patient appear adequate using the applicable criteria at 21 CFR 50 and 56 as guidelines (e.g., minimization of risks, risk/benefit, safety monitoring, informed consent, etc.).

The emergency use must be reported to the FDA by the IDE Sponsor, when one exists, or by the provider if no IDE exists. Information regarding what to include in the report and where to submit it is available on FDA's website. When the provider is responsible for the FDA report, a copy of the report and any related correspondence must be submitted to ORC.

Reports of emergency use will be brought to the convened IRB for their information.

Providers are reminded that they must comply with all other organizational policies and requirements applicable to the use of the investigational or unapproved devices.

7.6 Charging Subjects for Investigational Products

FDA regulations do not prohibit charging subjects or their insurers for investigational products so long as those charges comply with specified criteria. FDA approval of such charges does not obviate the investigator's and IRB's responsibility to minimize risks to subjects (Beneficence), to ensure that the risks and burdens associated with research are equitably distributed (Justice), and to ensure that subjects are properly informed and not unduly influenced to accept an otherwise

unacceptable risk or cost in order to access a benefit (Respect for Persons). Any costs to subjects or insurers must be described in the IRB application and informed consent document.

7.6.1 Charging for Investigational Medical Devices and Radiological Health Products

IDE regulations allow sponsors to charge for an investigational device, however, the charge may not exceed the amount necessary to recover the costs of manufacture, research, development, and handling of the investigational device [21 CFR 812.7(b)]. Sponsors must justify the proposed charges for the device in the IDE application, state the amount to be charged, and explain why the charge does not constitute commercialization [21 CFR 812.20(b)(8)].

7.6.2 Charging for Investigational Drugs and Biologics

In 2009, FDA updated its rules at 21 CFR 312 regarding charging for Investigational Drugs Under an IDE. These rules:

- Provide general criteria for authorizing charging for an investigational drug [21 CFR 312.8(a)]
- Provide criteria for charging for an investigational drug in a clinical trial [21 CFR 312.8(b)]
- Set forth criteria for charging for an investigational drug for an expanded access for treatment use [21 CFR 312.8(c)]
- Establish criteria for determining what costs can be recovered when charging for an investigational drug [21 CFR 312.8(d)]

Additional information is available in FDA guidance: Charging for Investigational Drugs Under an IND — Questions and Answers.

7.7 Responsibilities for FDA-Regulated Research

7.7.1 Principal Investigators ("Clinical Investigators")

7.7.1.1 General

1. Under FDA regulations and guidance, clinical investigators must be qualified by training and experience. They are responsible for the conduct of the study and for leading the team of individuals conducting the study. Before beginning participation in a clinical investigation, the clinical investigator must commit to the sponsor that he/she will follow federal regulations governing investigational drugs (including biologics) and devices.
2. Ensuring the informed consent is obtained from subjects in accordance with IRB approval

3. Retaining records for two years following the date the marketing application is approved by FDA or withdrawn and making those records available for inspection
4. Furnishing the required reports to the sponsor, including reports of adverse events and study completion
5. Providing timely reports to the IRB, including reports of changes in the research activity needed to avoid immediate hazards to participants, protocol deviations, unanticipated problems involving risks to participants or others (see Section 8 of these SOPs)
6. Informing any potential participants that the test article(s) (i.e., drugs) are being used for investigational purposes and ensuring that the requirements relating to obtaining informed consent and IRB review and approval are met
7. Ensuring that changes are not implemented without prospective IRB approval, unless required to eliminate immediate hazard to participants
8. Complying with the requirements of the Controlled Substances Act
9. Complying with all FDA test article requirements
10. Adequately maintaining control of test articles, including appropriate tracking documentation for test articles to the extent that such control and documentation are not centrally administered
11. Supervising the use and disposition of the test article
12. Disclosing relevant financial information and conflicts of interest
13. Ensuring that all associates, colleagues, and employees assisting in the conduct of the investigation(s) are informed about their obligations in meeting the above commitments.

NOTE: Principal Investigators cannot participate as subjects in their own studies.

7.7.1.2 Drug/Biologic Research

1. The clinical investigator must comply with the requirements specified in FDA Form 1572:

- Personally conduct or supervise the described investigation(s).
- Conduct the studies in accordance with the current IRB-approved protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, the rights, or welfare of participants.
- Comply with all requirements regarding the obligations of clinical investigators and all other pertinent regulatory requirements.
- Immediately report to the sponsor any serious adverse event, whether or not considered drug related, including those listed in the protocol or investigator brochure and must include an assessment of whether there is a reasonable possibility that the drug caused the event. Study endpoints that are serious adverse events (e.g., all-cause mortality) must be reported in accordance with the protocol unless there is evidence suggesting a causal relationship between the drug and the event (e.g., death from anaphylaxis). In that case, the investigator must immediately report the event to the sponsor.

The investigator must record nonserious adverse events and report them to the sponsor according to the timetable for reporting specified in the protocol. §312.64; (b)

- Read and understand the information in the investigator's brochure, including the potential risks and side effects of the drug.
- Ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.
- Ensure that an investigation is conducted according to the signed statement (Form FDA 1572), the investigational plan, and applicable regulations.
- Protecting the rights, safety, and welfare of participants under the clinical investigator's care.

2. The clinical investigator proposing drug/biologic research will be required to comply with the University's Investigational Drug Service plan for storage, security, and dispensing of the drug/biologics, and will be responsible for accounting, return, disposition, and records of accountability per the study protocol.

- For research conducted in the University Hospital, Health Sciences Center, Cancer Center, and Ambulatory Surgery Building, The PI will delegate the responsibility for drugs/biologics accountability, including storage, dispensing, labeling, and distribution, to the Investigational Drug Service in the Pharmacy Department.
- For research conducted in any other campus site, the plan will be provided to, and evaluated by the IRB, in consultation with the Investigational Drug Service at the time of submission review.
- The PI conducting investigational drug studies is required to share the study for ancillary review in the electronic management system with the Investigational Drug Service so that status of the IRB approval can be monitored and confirmed.
- The PI must inform the IRB and Pharmacy Service when a study involving investigational drugs has been terminated by the sponsor.

3. The clinical investigator will administer the drug only to participants under the clinical investigator's personal supervision or under the supervision of a sub-investigator responsible to the clinical investigator.
4. The clinical investigator will not supply the investigational drug to any person not authorized to receive it.
5. The clinical investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by participants (in accordance with any requirements set forth by the Investigational Drug Service).
6. If the investigation is terminated, suspended, discontinued, or completed, the clinical investigator must return the unused supplies of the drug to the sponsor, or otherwise provide for disposition of the unused supplies of the drug if authorized by the sponsor.

7. A clinical investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.
- Case histories include the case report forms and supporting data (e.g., signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes).The case history for each individual will document that informed consent was obtained prior to participation in the study.

8. A clinical investigator must retain records for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified. [21 CFR §312.62]
9. A clinical Investigator must maintain the following:

- Current curriculum vitae (CV)
- Protocol
- Records of receipt and disposition of drugs
- List of any co-investigators with their curriculum vitae
- Certification that all physicians, dentists, and/or nurses responsible in the study have appropriate valid licenses for the duration of the investigation, and
- Case histories with particular documentation on evidence of drug effects. Emphasis is on toxicity and possible untoward happenings. All unanticipated problems involving risk to subjects or others are reportable, in accordance with Section 8.
- IRB letters of approval.
- Other documents as outlined in the Human Research Protection Program Standard Operating Procedures.

7.7.1.3 Device Research

1. The clinical investigator must sign an agreement with the sponsor that includes a statement of the clinical investigator's commitment to: [21 CFR §812.43(c)(4)]

- Conduct the investigation in accordance with the agreement, the investigational plan, applicable FDA regulations, and conditions of approval imposed by the reviewing IRB or FDA;
- Supervise all testing of the device involving human participants; and
- Ensure that the requirements for obtaining informed consent are met.

2. The clinical investigator must ensure that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations
3. The Clinical Investigator is responsible for the control of devices under investigation and will therefore be required to provide a plan – to be evaluated by the IRB - that includes storage, security, and dispensing of the device, and will be responsible for accounting, return,

disposition, and records of accountability per the study protocol. If the IRB determines that it does not have the necessary expertise to evaluate the plan, outside consultation will be used (e.g., Biomedical Engineering).

4. All devices received for a study must be stored in a locked environment under secure control with limited access. The area must be within an area of PI's control. Proper instructions on the use of the device must be provided to the subjects. A log must be kept regarding the receipt, use, and/or dispensing of the device (identification/serial number of the device, name of subject, date dispensed, by whom it was dispensed, and amount remaining) as well as the disposition of used and unused devices at the conclusion of the investigation. Details: [21 CFR §812.140] VIT D2 1.25 MG The clinical Investigator will maintain records of each participant's case history and exposure to the device. Case histories include the case report forms and supporting data (e.g., signed and dated consent forms and medical records, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes). Such records will include:

- Documents evidencing informed consent and, for any use of a device by the clinical investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The case history for each individual will document that informed consent was obtained prior to participation in the study.
- All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each participant upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
- A record of the exposure of each participant to the investigational device, including the date and time of each use, and any other therapy.
- The protocol, with documents showing the dates of and reasons for each deviation from the protocol.
- Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

5. Device investigators must report to the sponsor and the SBU IRB:

- Unanticipated adverse device effects
- Withdrawal of IRB approval
- Reports of deviations from the approved investigational plan
- Progress reports (at least annually) and a final report
- Other reports as required/requested by the sponsor or IRB

6. If a device is considered NSR by the PI or sponsor, but after review the IRB determines the device to have significant risk, upon receipt of written notice the PI is responsible for notifying the sponsor of the IRB's determination. The PI must provide the IRB with confirmation of this action.

7. The PI will maintain the following:

- Current curriculum vitae (CV),
- Protocol of the study,
- Records of animal study reports
- Records of receipt and disposition of devices
- List of any co-investigators with their curriculum vitae,
- Certification that all physicians, dentists, and/or nurses responsible in the study have appropriate valid licenses for the duration of the investigation,
- Case histories with particular documentation on evidence of effects. Emphasis is on safety and possible untoward happenings. All unanticipated adverse device effects are reportable, per Section 8, SOPs
- IRB letters of approval
- Device training.
- Other documents as required in these Standard Operating Procedures.

7.7.1.4 *Additional* Responsibilities When the Clinical Investigator is also the Sponsor of the IND or IDE ("Sponsor-Investigator")

These studies in question are typically investigator-initiated studies that use an investigational drug or device or use an approved drug or device for investigational purposes.

1. Sponsors-Investigators: General

- The investigator has both investigator responsibilities (as above), and sponsor responsibilities, which include:
  - Selecting qualified investigators;
  - Providing investigators with the information they need to conduct the investigation properly;
  - Ensuring proper monitoring of the investigation and document monitoring activities;
  - Ensuring that the FDA and (for devices) any reviewing IRBs or (for drugs) all participating investigators are promptly informed of significant new information about an investigation; and
  - Reporting requirements to the FDA.
- Sponsor-investigators who submit protocols to SBU's IRB involving FDA test articles must include supporting FDA documentation for their IND or IDE.
- If the IND or IDE product will be manufactured at Stony Brook University, the clinical investigator must submit documentation that the product preparation and manufacture meets the standards for current Good Manufacturing Practice (GMP), or any modification to those standards approved by the FDA in

issuing the IND or IDE. This documentation will be subject to review by appropriate SBU entities, as determined by the Office of Research Compliance.

- The IND or IDE product must be stored, secured, dispensed, and documented as indicated in the submission materials to the IRB, and in accordance with the requirements referenced in the preceding sections.
- Comply with the University Support Services submission requirements below (See section 7.5.1.5 below)

2. Sponsors-Investigators: IDE's

- A sponsor-investigator for an IDE protocol must follow the FDA regulations in 21 CFR 812 applicable to sponsor responsibilities, particularly Subpart C. This includes:
  - The record keeping requirements of 21 CFR 812.140(b), and
  - The required notification under 21 CFR 812.150(b)(1) to the FDA an all participating investigators of any evaluation of an unanticipated device effect within 10 days of first receiving notice of the effect.
- An investigation of a device other than a significant risk device is considered to have an approved application for IDE, unless FDA has given notice under 812.20(a) that approval of an application is required, if the device is not a banned device and the sponsor:
  i. Labels the device in accordance with 812.5;
  ii. Obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval;
  iii. (Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under part 50 and documents it, unless documentation is waived by an IRB under 56.109(c).
  iv. Complies with the requirements of 812.46 with respect to monitoring investigations;
  v. Maintains the records required under 812.140(b) (4) and (5) and makes the reports required under 812.150(b) (1) through (3) and (5) through (10);
  vi. Ensures that participating investigators maintain the records required by 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7); and
  vii. Complies with the prohibitions in 812.7 against promotion and other practices.

3. Sponsor-Investigators: IND's

- A sponsor-investigator for an IND protocol must follow the FDA regulations in 21 CFR 312 applicable to sponsor responsibilities, particularly Subpart D. This includes:
  - The record keeping requirements of 21 CFR 312.57, and
  - Promptly reporting as required in 21 CFR 312.55(b) to the FDA and all participating investigators of significant new adverse effects or risks with respect to the drug or biologic.

4. FDA regulations for investigators assuming the sponsor function by holding an IND or IDE

Drugs or devices:

* 21 CFR §11 (Electronic records and electronic signature)

* 21 CFR §54 (Financial Disclosure by Clinical Investigators)

Drugs and Biologics:

* 21 CFR §210 (Current Good Manufacturing Practice In Manufacturing, Processing, Packing, Or Holding of Drugs; General)

* 21 CFR §211 (Current Good Manufacturing Practice for Finished Pharmaceuticals)

* 21 CFR §312 (Investigational New Drug Application)

* 21 CFR §314 (Drugs for Human Use)

* 21 CFR §320 (Bioavailability and Bioequivalence Requirements)

* 21 CFR §330 (Over-The-Counter (OTC) Human Drugs Which are Generally Recognized as Safe and Effective and Not Misbranded)

* 21 CFR §601 (Biologics Licensing)

Devices:

* 21 CFR §812 (Establishment Registration and Device Listing for Manufacturers and Initial Importers of Devices)

* 21 CFR §812 (Investigational Device Exemptions)

* 21 CFR §814 (Premarket Approval of Medical Devices)

* 21 CFR §820 (Quality System Regulation)

* 21 CFR §860 (Medical Device Classification Procedures)

7.7.1.5 University Support Services for Sponsor-Investigators

The Office of Research Compliance provides support services for investigators who also act as a Sponsor of INDs (and IND-BB's), and IDEs. Regulatory support includes guidance and assistance on pre-submission FDA interactions, IND and IDE submissions and associated reports to the FDA and the IRB.

The following assistance is provided upon request:

- Determination of applicability of an IND or IDE (IRB oversight continues to apply)
- Training in the obligations of a sponsor-investigator
- Pre-IND, IDE consultation with FDA and participation in on-going communication with the agency as required
- Assistance with submission of IND, IDE to FDA to ensure all required forms are included.
- Assistance with fulfilling IND reporting requirements to ensure the study is conducted according to the current approved protocol.

The University has accountability obligations for all sponsor-investigator drug, device, or biologic research at the University. **To promote compliance with FDA, IND, and IDE regulations the following documents must be submitted with the IRB protocol through the electronic management system and shared with the IND Administrator for Ancillary Review:**

- FDA Form 1571 – Investigational New Drug Application
- FDA Form 1572 – Statement of Investigator
- FDA Form 3674 – Certificate of Compliance

Or

- FDA Form 3926 – Individual Patient Expanded Access Application with Physician CV to confirm qualifications
- IND Annual renewal report
- Copy of SAE report within 3 days of submission to FDA

7.7.2 IRB

1. The IRB will review the research in accordance with the following requirements and the same criteria it would use in considering approval of any research involving an FDA-regulated product (21 CFR 56.111).
2. For research involving investigational devices:
   Unless the FDA has already made a risk determination for the study, the IRB will review NSR studies and determine if the device represents significant or non-significant risk and will document its findings. The IRB will consider the risks and benefits of the medical device compared to the risks and benefits of alternative devices or procedures. Non-significant risk device studies do not require submission of an IDE application but must be conducted in accordance with the abbreviated requirements of IDE regulations:

- The device is not a banned device.
- The sponsor labels the device in accordance with 21 CFR 812.5.

- The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device was not a significant risk device, and maintains such approval.
- The sponsor ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, consent under 21 CFR 50 and documents it, unless documentation was waived.
- The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations.
- The sponsor maintains the records required under 21 CFR 812.140(b)(4) and (5) and makes the reports required under 21 CFR 812.150 (b)(1) through (3) and (5) through (10).
- The sponsor ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 812.150(a)(1), (2), (5) and (7).
- The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.
- If the study that has been submitted as NSR is considered SR, the IRB may approve the study, but the study cannot begin until an IDE is obtained.

3. The IRB will not review protocols involving significant risk devices under expedited review.
4. The IRB will document in the minutes the rationale for determining whether a device is classified as NSR/SR.
5. If the FDA has already made the SR or NSR determination for the study, the agency's determination is final and the IRB does not need to make a risk determination.

7.8 Policy on Research with Dietary Supplements

Research involving dietary supplements may or may not fall under FDA regulations. Under the Dietary Supplement Health and Education Act (DSHEA) of 1994, a dietary supplement is not considered a drug and is not subject to the premarket approval requirements for drugs if the intended use for which it is marketed is only to affect the structure or any function of the body (i.e., not intended to be used for a therapeutic purpose). Whether a study falls under FDA oversight is determined by the intent of the clinical investigation. If the clinical investigation is intended only to evaluate the dietary supplement's effect on the structure or function of the body, FDA research regulations do not apply. However, if the study is intended to evaluate the dietary supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease, then FDA regulations do apply. Studies involving the ingestion of dietary supplements that are not subject to FDA oversight are still research, and therefore must be reviewed by the IRB.

Similarly, whether an IND is needed for a study evaluating a dietary supplement is determined by the intent of the study. If the study is intended only to evaluate the dietary supplement's effect on the structure or function of the body, an IND is not required. However, if the study is intended to

evaluate the dietary supplement's ability to diagnose, cure, mitigate, treat, or prevent a disease, an IND is required under part 312.

As with any research involving a test article, the investigator must supply the IRB with sufficient information to determine that the criteria for approval are satisfied and to determine or verify whether the research requires an IND. Applications should provide detail consistent with that expected on a drug protocol and consistent with the level of risk associated or anticipated with the research. At a minimum, the research plan should provide the following information regarding the supplement: Name, Manufacturer, Formulation, Dosage, Method/Route of Administration, Mechanism of Action, Known Drug Interactions, Risk Profile, IND number (or justification for why an IND is unnecessary), documentation of approval for use in humans, documentation or certification of Quality or Purity. As with drugs and devices there should be an accountability plan for the product describing where the product will be stored and how it will be dispensed, usage tracked, and disposal or return. If the study entails greater than minimal risk, a plan for Data and Safety Monitoring must be included.

8 Unanticipated Problems Involving Risks to Subjects or Others (a type of 'Reportable New Information-RNI')

8.1 Policy

The University complies with DHHS and FDA regulations which state that institutions must have written policies on reporting unanticipated problems involving risks to subjects or others to the IRB, institutional officials and relevant federal agencies and departments.

8.2 Definitions

Unanticipated Problem Involving Risk to Subjects or Others: refers to any problem, event, or new information that:

1. Is unexpected (in terms of nature, severity, or frequency) given the research procedures that are described in the protocol-related documents, such as the IRB approved research protocol and informed consent documents; and the characteristics of the subject population being studied; and
2. Indicates that subjects or others are at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.
3. Is possibly or probably related to the research procedures described in the protocol-related documents.

Note: Unanticipated problems occurring in subjects whose participation in the study ended within 30 days of the unanticipated problems are considered applicable to this policy

Adverse Event (AE): Any untoward physical or psychological occurrence in a human subject participating in research. An AE can be any unfavorable or unintended event including abnormal laboratory finding, symptom or disease associated with the research or the use of a medical investigational test article.

Serious Adverse Event (SAE): A life threatening experience; hospitalization (for a person not already hospitalized); prolongation of hospitalization (for a patient already hospitalized); persistent or significant disability or incapacity; congenital anomaly and/or birth defects; or an event that jeopardizes the subject and may require medical or surgical treatment to prevent one of the preceding outcomes.

Unexpected Adverse Event (UAE): Any adverse event and/or reaction, the specificity or severity of which is not consistent with the informed consent, current investigator brochure or product labeling. Further, it is not consistent with the risk information described in the general investigational plan or proposal.

Adverse Device Effect (ADE): Any adverse event/effect caused by or associated with the use of a device that is unanticipated and has not been included in the protocol or the Investigator's Brochure.

Related: An event is "related" if it is likely to have been caused by the research procedures.

Unexpected Death: The death of a research subject in which a high risk of death is not projected, as indicated by the written protocol, informed consent form, or sponsor brochure. This definition does not include deaths associated with a terminal condition unless the research intervention clearly hastened the subject's death. A subject's death that is determined to be clearly not associated with the research is also not an "unexpected death" for purposes of the reporting requirements of these procedures.

8.3 Procedures

The following procedures describe how unanticipated problems involving risk to subjects or others are handled in research conducted under the auspices of the University.

8.3.1 What must be reported

Investigators must report the following problems to the IRB (see Section 8.3.2 for timelines)

1. Serious adverse events which in the opinion of the principal investigator are both unexpected and related to the research activity.

2. Adverse events (other than SAEs) which in the opinion of the principal investigator meet the criteria for an unanticipated problem involving risk to subjects or others (unanticipated, related to the research and increase risk to subjects).
3. An unanticipated event related to the research that exposes subjects to potential risk.
4. An unanticipated event related to the research that exposes individuals other than the research subjects (e.g., investigators, research assistants, students, the public, etc.) to potential risk.
5. Information that indicates a change to the risks or potential benefits of the research. For example:
    - An interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than initially presented to the IRB.
    - A paper is published from another study that shows that the risks or potential benefits of the research may be different than initially presented to the IRB.
6. A breach of confidentiality.
7. Incarceration of a subject in a protocol not approved to enroll prisoners.
8. Changes increasing the risk to subjects and/or significantly affecting the conduct of the trial.
9. Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research subject.
10. Complaint of a subject when the complaint indicates unexpected risks or cannot be resolved by the research team.
11. Protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) that harmed subjects or others or that indicates subjects or others may be at increased risk of harm.
12. Event that requires prompt reporting to the sponsor.
13. Sponsor imposed suspension for risk.
14. Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
15. Unanticipated adverse device effect - Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects (21 CFR 812.150(a).

Any other event that indicates subject or others might be at risk of serious, unanticipated harms that are reasonably related to the research.

8.3.2 Report Filing Deadlines

Unanticipated Problem ('Reportable New Information') Reports should be submitted to ORC as soon as possible after they have occurred, but within **five (5) working days** of occurrence, or of receipt by University Investigator (if non-University subject).

Problems/AE's/SAE's that occur that are anticipated should be submitted as a cumulative summary report (by sponsor, if applicable) required at time of Continuing Review.

8.3.3 IRB Procedures for Handling Reports of Possible Unanticipated Problems

8.3.3.1 Review of Unanticipated Problem Reports: University Subjects

Unanticipated Problem Reports will be reviewed by IRB staff to confirm that the reported incident constitutes an unanticipated problem (in consultation with the IRB Chair or AVP-RC, as needed), and will make an initial determination regarding action.

If it is determined that immediate action may be required, the unanticipated problem will be forwarded to the chair for review. If the IRB Chair deems it necessary to take action before the IRB meeting (e.g., suspension etc.), the PI will be notified regarding steps to be taken to ensure protection of rights/welfare of subjects (or staff, as appropriate), pending review and action by the full committee. If the IRB Chair is not available, the AVP-RC or the IO will make the determination regarding immediate actions to be taken to protect subjects. If immediate action is not required, the unanticipated problem will be placed in the agenda for full review at the next IRB meeting. Pre-review may be conducted by one (1) or more IRB members. All members will receive the study documents.

8.3.3.2 Review of UP Reports: Non-SBU Subjects

Unanticipated Problem Reports concerning subjects or others not enrolled through the University will be reviewed by IRB staff. If the definition of a UP is met, review will be conducted to confirm that sponsor and FDA have been notified (per unanticipated problem (UP)/USAE form). OHRP will be notified by the IO per the requirements of the FWA, and the report and study history will be placed on the agenda for the applicable IRB meeting.

If regarding a study with External IRB oversight, the report will be placed on the next available meeting agenda and the form will be filed in the applicable IRB file. ORC reviewer may, at his/her discretion, send the USAE to an IRB member or full committee for review. An acknowledgement letter regarding these submitted USAE's will not be sent to PI unless the IRB determines that further action or clarification is required.

8.3.4 Review Outcomes

1. If the IRB finds that the event is an unanticipated problem involving risks to subjects or others, according to the definition in the policy, the IRB may recommend any of the following actions:

- Requiring modifications to the protocol
- Revising the continuing review timetable
- Modifying the consent process
- Modifying the consent document
- Providing additional information to current subjects (e.g. whenever the information may relate to the subject's willingness to continue participation)
- Providing additional information to past subjects
- Requiring additional training of the investigator and/or study staff
- Reconsidering approval
- Requirement that current subject's re-consent to participation
- Monitoring of the research
- Monitoring of the consent
- Referral to other organizational entities in writing (e.g., legal counsel, risk management, institutional official)
- Suspending the research
- Terminating the research
- Other actions appropriate for the local context

2. If a report suggests that subject safety is at risk, the IRB may immediately suspend or terminate the research. Any suspension or termination of research by the IRB will be promptly reported in writing to OHRP, and FDA (if FDA-regulated research) by the IO.
3. If, after reviewing a report, the IRB finds that the event is an unanticipated problem involving risks to subjects or others or that suspension or termination of approval is warranted, the IRB will:

- Notify the investigator in writing of its findings, with copies to the chair of the investigator's department and/or research unit, and the investigator's supervisor; and
- Report its findings and recommendations to the IO for further reporting to the appropriate federal officials as applicable (OHRP, and FDA).

Any unanticipated problems involving risks to subjects or others occurring in DoD-supported research will be reported within thirty (30) days to the DoD human research protection officer.

9 Protocol Exceptions or Deviations

9.1 Policy

It is the policy of the IRB to be notified of any protocol deviations or exceptions that result in an increase in risk or a decrease in benefit to subjects.

The following procedures describe how protocol exceptions and deviations are reported to the IRB.

9.2 Protocol Exceptions

Protocol exceptions: Circumstances in which the specific procedures called for in a protocol are not in the best interests of a specific subject (e.g. subject is allergic to one of the medications provided as supportive care).

Exceptions are planned, and the investigator gets approval from the sponsor and the IRB ahead of time. These should be submitted in the electronic management system. Depending on the nature of the exception, an expedited review is possible. In order to be approved by the IRB, exceptions must not increase risk or decrease benefit, affect the subject's rights, safety, welfare, or affect the integrity of the resulting data.

The only time a protocol exception would not require prior sponsor and IRB approval is when it is done to avoid an immediate hazard to the subject. The above application should be used to report the incident for IRB review.

9.3 Protocol Deviations (a type of 'Reportable New Information; RNI')

Protocol deviations: Circumstances that are unanticipated and happen without any prior sponsor or IRB approval. (e.g. protocol visit scheduled outside protocol window, blood work drawn outside protocol window, etc.).

All deviations:

- Must be reported to ORC (unless the deviation consists of minor scheduling deviations of study visits that are unavoidable and do not impact subject safety) in the electronic management system.
- Are reviewed to determine if they:
  - Are minor, and don't impact subject safety (these are acknowledged by ORC), or
  - Constitute noncompliance. In these cases, the deviations would be reviewed by the IRB for determination of non-serious, serious, or continuing noncompliance; the latter 2 must be reported to OHRP, and other federal agencies (e.g. FDA etc.) and sponsors (as applicable), and/or

- Constitute unanticipated problems involving risks to subjects or others (UP). In these cases, the deviations are reviewed by the IRB for confirmation of UP status. If confirmed, they must be reported to OHRP, other federal agencies (e.g. FDA, etc.) and sponsors (as applicable). See section 8 for additional information on UPs.

9.4 Reporting & Review

The IRB staff will review the submitted information, and either process for expedited review, IRB chair review, or full committee review as applicable. Outcome of review will be uploaded into the electronic management system for investigator review and action, if necessary. If the information provided is of serious concern, the staff will involve the Chair and/or AVP-RC and/or IO as soon as possible, before the IRB meeting, for any action deemed necessary to protect enrolled subjects.

10 Complaints and Non-compliance (types of 'Reportable New Information- RNI')

10.1 Policy

As part of its commitment to protect the rights, safety, and welfare of human subjects in research, the University reviews all complaints and allegations of non-compliance and takes any necessary action to ensure the ethical conduct of research.

The following procedures describe how complaints and allegations of non-compliance are handled by the IRB.

10.2 Definitions

Non-compliance: Failure to comply with any of the regulations and policies described in this document and/or failure to follow the determinations of the IRB. Non-compliance may be minor or sporadic or it may be serious or continuing.

Serious non-compliance: Failure to follow regulations and policies described in this document or failure to follow the determinations of the IRB and which, in the judgment of either the IRB Chair or the convened IRB, increases risks to subjects, decreases potential benefits, or compromises the integrity of the human research protection program. Non-exempt research being conducted without prior IRB approval, or participation of subjects in research activities without their prior consent (in studies where consent was not specifically waived by the IRB) is always considered serious noncompliance.

Continuing Non-compliance: A pattern of non-compliance that, in the judgment of the IRB Chair or convened IRB, suggests a likelihood that instances of non-compliance will continue without

intervention, or where instances of non-compliance **have** continued even where intervention by the IRB has occurred. Continuing non-compliance also includes failure to respond to a request to resolve an episode of non-compliance.

Allegation of Non-Compliance: An unproved assertion of non-compliance.

Finding of Non-Compliance: An allegation of non-compliance that is proven true or a report of non-compliance that is clearly true. (i.e. a finding on an audit of an unsigned consent document, or an admission of an investigator of that the protocol was willfully not followed would represent reports of non-compliance that would require no further action to determine their truth and would therefore represent findings of non-compliance). Once a finding of non-compliance is proven, it must be categorized as serious, non-serious, or continuing.

10.3 Complaints

Complaints and concerns received by ORC from investigators, subjects, and others will be reviewed, in consultation with the IRB Chair, AVP-RC and/or IO as applicable. Upon referral to the IRB Chair she/he will make a preliminary assessment whether the complaint warrants immediate suspension of the research project. If a suspension is warranted, the procedures in Section 3.11.1 will be followed.

If the complaint meets the definition of non-compliance, it will be considered an allegation of non-compliance according to Section 10.4

If the complaint meets the definition of an unanticipated problem involving risk to subjects or others, it will be handled according to Section 8.

10.4 Non-compliance

Investigators and their study staff are required to report instances of possible non-compliance. The PI is responsible for reporting any possible non-compliance by study personnel to the ORC. Any individual or employee may report observed or apparent instances of noncompliance to the ORC. In such cases, the reporting party is responsible for making these reports in good faith, maintaining confidentiality and cooperating with any ORC, IRB, and/or institutional review of these reports.

If an individual, whether investigator, study staff or other, is uncertain whether there is cause to report noncompliance, he or she may contact the ORC staff to discuss the situation informally.

Reports of non-compliance must be submitted to the ORC **within ten (10) working days** of discovery of the noncompliance. The report may be verbal or written, and must include a complete description of the noncompliance, and the personnel involved. Complainants may choose to remain anonymous.

10.4.1 Review of Allegations of Non-compliance

Allegations of non-compliance will be pre-reviewed by the IRB Chair for merit. Where the allegation involves multiple studies, or a study with off-site IRB oversight, the IRB will conduct the review during the next scheduled meeting. The IRB Chair will consider all documents relevant to the allegation, and all documents pertaining to the study (available in the electronic management system). The Chair upon initial review of the allegation will determine whether the allegation has a basis in fact. Where there exists a situation in which the noncompliance may affect subject safety, the IRB Chair and (in his or her absence), the AVP-RC or the IO are empowered to require immediate, appropriate action (e.g. study suspension, enrollment suspension) prior to full committee review.

Allegations of non-compliance deemed by the IRB chair to have merit will be brought to the next meeting of the full committee for review. Where the allegation is made against a specific individual, that individual will be notified that an allegation of non-compliance has been made against him/her by the IRB Chair or ORC staff, and will be given opportunity to respond before the meeting, if possible.

The IRB will review the allegation and make a determination as to the truthfulness of the allegation. In addition to possibly requesting more information from the reporting party, the IRB may determine that additional expertise or assistance is required to make these determinations and may form an ad hoc committee to audit the research in question, or assist with the review and fact gathering process. The ad hoc committee results are transmitted via a written report to be read at a convened meeting, or the report can be verbal, where the ad hoc committee consists of ORC staff and/or IRB members.

When a determination is made that that noncompliance did not occur because the incident was within the limits of an approved protocol for the research involved, the determination is reported in writing to the PI and the reporting party (if applicable). The determination letter will be copied to the IO in cases where the IO and any other parties had been notified at the outset.

If a determination is made that the reported allegation of non-compliance is true, the non-compliance will be processed according to Section 10.4.2 Review of Findings of Non-compliance.

10.4.2 Review of Findings of Non-compliance

Noncompliance is not serious or continuing:

When the IRB determines that the noncompliance occurred, but the noncompliance does not meet definition of serious or continuing noncompliance, the determination is reported in writing to the PI (and if applicable the reporting party) by the ORC staff, with the requirement for the development of a corrective action plan, as deemed necessary, to prevent future noncompliance. If the PI refuses to cooperative with the corrective action plan, the matter is referred to a convened meeting of the IRB with notification to the IO if deemed appropriate.

Serious or Continuing Noncompliance

Documents will be sent to all members of the IRB. When the IRB determines that noncompliance has occurred and that the noncompliance meets the definition of serious or continuing noncompliance, they may:

1. Require submission of a corrective action plan from the PI;
2. Require re-training in human subject protections;
3. Direct that a for-cause (directed) audit be conducted of all the PI's research activities, and/or;
4. Notification of appropriate institutional officials in cases where other University policies may have been violated (e.g. scholarly misconduct, financial disclosure/COI, etc.);
5. Increase in data and safety monitoring of the research activity;
6. Request a status report after each subject receives intervention
7. Modify the study's continuing review cycle;
8. Notify current subjects, if the information about the non-compliance might affect their willingness to continue participation;
9. Require modification of the protocol;
10. Require modification of the information disclosed during the consent process;
11. Require current subjects to re-consent to participation;
12. Suspend the study (See below); or
13. Terminate the study (See below)

In cases where the IRB determines that the event of noncompliance also meets the definition of unanticipated problem involving risks to subjects or others, the policy and procedure for review of such events will also be followed. The investigator is informed of the IRB determination and the basis for the determination in writing.

11 Reporting to Regulatory Agencies and Institutional Officials

11.1 Policy

Federal regulations require prompt reporting to appropriate institutional officials, and the department or agency head of (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB; and (ii) any suspension or termination of the IRB approval. Stony Brook University HRPP will comply with this requirement and the following procedures describe how these reports are handled.

11.2 Procedures

1. The IRB staff will notify the IO of 'reportable' determinations by the IRBs (i.e., unanticipated problems involving risks to subjects or others, serious/continuing non-compliance, suspensions, terminations) as soon as possible after the meeting in question.
2. The IO or designee is responsible for preparing reports or letters which includes the following information. The report will be sent within 30 days. The maximum time allowed between the recognition of the reportable event and fulfilling reporting requirements is 180 days:

- The nature of the event (unanticipated problem involving risks to subjects or others, serious or continuing non-compliance, suspension or termination of approval of research);
- Title of the research project and/or grant proposal in which the problem occurred;
- Name of the principal investigator on the protocol;
- Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
- A detailed description of the problem including the findings of the organization and the reasons for the IRB's decision;
- Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.); and
- Plans, if any, to send a follow-up or final report by the earlier of
  - A specific date, or
  - When an investigation has been completed or a corrective action plan has been implemented.

3. The IO is the signatory for all correspondence from the University.
4. The IO or designee sends a copy of the report to the following federal agencies:

- OHRP, if the study is subject to DHHS regulations or subject to a DHHS federalwide assurance.
- If the study is conducted or supported by a Common Rule agency other than DHHS, the report is sent to OHRP or the head of the federal agency, as required by the agency.
- If the study is conducted or supported by a federal agency that has not adopted the Common Rule, and reporting is required, the report is sent to the party identified by the agency.

- FDA, if the study is subject to FDA regulations.
- Others as deemed appropriate by the IO.

Reports are **not submitted** to federal departments or agencies such as OHRP or FDA unless the research is subject to federal regulations or another mandate that necessitates such reporting.

Note: Reporting to a regulatory agency is not required if the event occurred at a site that was not subject to the direct oversight of the organization, and the agency has been notified of the event by another party (e.g., sponsor).

SBU's Human Research Protection Program is accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP). In addition to the information that AAHRPP routinely provides to AAHRPP in annual reports and the re-accreditation application, AAHRPP requires that any of the following are reported to AAHRPP as soon as possible but generally within 48 hours after the organization or any researcher (if the researcher is notified rather than the organization) becomes aware:

- Any negative actions by a government oversight office, including, but not limited to, OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA Restrictions placed on IRBs or investigators, and corresponding compliance actions taken under non-US authorities related to human research protections;
- Any litigation, arbitration, or settlements initiated related to human research protections; and/or
- Any press coverage (including but not limited to radio, TV, newspaper, online publications) of a negative nature regarding SBU's HRPP.

The Associate Vice President for Research Compliance (or designee) is responsible for ensuring that such reports are made to AAHRPP and for informing appropriate organizational officials. Investigators, research staff, HRPP/IRB staff, IRB members, and other organizational officials or offices (e.g., the Institutional Official, legal counsel) are responsible for informing the ORC as soon as they become aware of any of the above so that these reporting obligations may be fulfilled.

The AVP-RC, on behalf of the IO ensures that all steps of this policy are completed within thirty (30) days of the convened IRB's determination of an unanticipated problem, serious or continuing noncompliance, suspension, or termination.

12 Investigator Responsibilities

12.1 Policy

Principal Investigators (PI) are ultimately responsible for the compliant and ethical conduct of research. Principal Investigators may delegate aspects of the research across the study team, consistent with specific requirements for licensures or training for specific procedures (i.e. performing venipuncture, administering medication). However, PIs must maintain oversight and retain ultimate responsibility for the conduct of those to whom they delegate responsibility.

The following procedures describe the investigator responsibilities in the conduct of research involving human subjects.

12.2 Investigators

12.2.1 Principal Investigators

Only **individuals holding a current faculty appointment** may serve as the PI on a research project involving human subjects. The IRB may, on a case-by-case basis, permit University staff to serve as PIs based on, but not limited to, the following criteria:

- The individual is not a student;
- Nature of the study; study must be deemed minimal risk to human subjects;
- The individual's training in conducting research involving human subjects;
- The individual's experience in conducting research involving human subjects;
- The individual's education level, masters or doctorate preferred;
- The individual's motivation in performing research (e.g. must not be doing the research toward a degree or certification);
- Approval and signatory certification of, and oversight by their supervisor.

Those wishing a waiver from the faculty PI requirement must address each criterion above, provide a resume/CV, and submit to the ORC for forwarding to the IRB for review. Only employees can request a waiver.

The IRB recognizes one PI for each study. The PI has ultimate responsibility for the research activities.

Protocols that require skills beyond those held by the PI must be modified to meet the investigator's skills or have one or more additional qualified faculty as co-investigator(s).

There must be adequate resources to carry out the research safely. This includes, but is not limited to, sufficient researcher time, appropriately qualified research team members, equipment, and space.

12.2.2 Student Investigators

Students may not serve as PIs. They must have a faculty sponsor who fulfills the PI eligibility criteria and who will serve as PI and faculty advisor on the study.

12.2.3 Research Team

The research team consists of individuals who intervene or interact directly with subjects (including the recruitment or consenting thereof), or who analyze data and/or tissue derived from humans for the purposes of the activity in question.

12.3 Responsibilities

In order to satisfy the requirements of this policy, investigators who conduct research involving human subjects must:

1. Develop and conduct research that is in accordance with the ethical principles in the Belmont Report;
2. Develop a research plan that is scientifically sound and minimizes risk to the subjects;
3. Have sufficient resources necessary to protect human subjects, including:
   a) Access to a population that would allow recruitment of the required number of subjects.
   b) Sufficient time to conduct and complete the research.
   c) Adequate numbers of qualified staff.
   d) Adequate facilities.
   e) A process to ensure that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions.
   f) Availability of medical or psychological resources that subjects might require as a consequence of the research.
4. Assure that all procedures in a study are performed with the appropriate level of supervision and only by individuals who are licensed or otherwise qualified to perform such procedures under the laws of New York and the policies of SBU;
5. Assure that all key personnel are educated in the regulatory requirements regarding the conduct of research and the ethical principles upon which they are based;
6. Protect the rights and welfare of prospective subjects;
7. Ensure that risks to subjects are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii)

whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes;
8. Recruit subjects in a fair and equitable manner;
9. Obtain and document informed consent as required by the IRB and ensure that no research procedure is performed prior to obtaining and documenting consent from the human subject.;
10. Have plans to monitor the data collected for the safety of research subjects;
11. Protect the privacy of subjects and maintain the confidentiality of data;
12. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, include additional safeguards in the study to protect the rights and welfare of these subjects;
13. Have a procedure to receive complaints or requests for additional information from subjects and respond appropriately;
14. Ensure that pertinent laws, regulations, and institutional procedures and guidelines are observed by participating investigators and research staff;
15. Ensure that all research involving human subjects receives IRB review and approval in writing before beginning the research;
16. Comply with all the IRB decisions, conditions, and requirements;
17. Ensure that protocols receive timely continuing IRB review and approval (as applicable);
18. Report deviations, noncompliance, and unanticipated problems involving risks to subjects or others in accordance with these SOPs;
19. Obtain the IRB review and approval in writing before changes are made to approved protocols or consent forms, unless a change is necessary to eliminate apparent immediate hazards to the subject(s); and
20. Seek IRB assistance when in doubt about whether proposed research requires the IRB review.
21. Maintain records of drugs and devices that document adequately that the participants are provided the doses or device specified by the protocol and reconcile all investigational products received from the sponsor

12.4 Training/ Ongoing Education of Investigators and Research Team

As stated above, one component of a comprehensive human research protection program is an education and training for all individuals involved with human subjects. The University is committed to providing training and an on-going educational process for investigators and members of their research team related to ethical concerns and regulatory and institutional requirements for the protection of human subjects. As an example, initial and continuing research ethics education is required for all personnel who conduct, review, approve, oversee, support, or manage human subjects research sponsored by the Department of Defense.

Approval of new and continuing review submissions will be withheld unless all individuals listed in the electronic submission form as part of the study team are current in their certification to conduct human subject research, as defined in this document. ORC maintains the database of training certifications.

12.4.1 Initial Education

All PIs and members of their research team (including students) must:

- Review core training documentation including the "SBU Standard Operating Policies and Procedures for Human Research Protection" and the "Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research";
- Be familiar with the University HRPP website, and the availability of links and other information contained within;
- Complete the University-required Basic Modules in the CITI Course in the Protection of Human Research Subjects, and pass the required quizzes with a score of 80 or better. Refresher training must be completed every 3 years.

Additional training:

- Study Coordinators on file with the Office of Clinical Trials must satisfy a one-time completion of the CITI course on Clinical Research Coordinators (CRC)
- NIH-funded investigators and clinical trial site staff who are responsible for the conduct, management and oversight of NIH-funded clinical trials must complete training in GCP (every three years).

    - Individuals who are funded externally must take the following training for conflict of interest:
    - Required every 4 years
    - Education is required immediately when:
    - Financial conflict of interest policies are revised in a manner that changes research requirements
        - A researcher is new to the organization
        - A researcher is non-compliant with financial conflict of interest policies and procedures

12.4.1.1 The Collaborative Institutional Training Initiative (CITI)

The University offers access to the CITI program to all University faculty, staff, and students. Non-University investigators can use the CITI program if they are on file with the IRB as an investigator on an IRB application (approved or pending). **Unauthorized use of the CITI program is prohibited.**

The CITI web-based program is available at **http://www.citiprogram.org.** Investigators register under SUNY University at Stony Brook. After login, questions will be asked to assess what type of training is required based on certain criteria; it is the investigator's responsibility to choose the answers that most accurately addresses:

- Level of University training (initial, refresher);
- Type of research (biomedical, social behavioral); and
- Role in the research activities (data/tissues only, interaction with subjects, etc.).

Completion of the initial training through CITI takes approximately four to six (4-6) hours, although the trainee can go back over multiple sessions to complete training.

The Biomedical Research Alliance of New York (BRANY; which provides the IT, administrative support, and home to the CITI Program) issues CME/CEU credits for a fee. In order to qualify for CME/CEU credits, you must take and pass all required modules for the group you choose. Click the link for CME/CEU credits on the Learner's Menu for detailed information.

12.4.2 Waiver of Initial Education

If investigators or members of their research team are new to the University, and can verify that they have successfully completed the CITI training at their former institution (involving equivalent modules to that required by the University), they may request a waiver of that aspect of Initial Education. However, they still must confirm review of the "SBU Standard Operating Policies and Procedures for Human Research Protection" and website materials.

12.4.3 Continuing Education and Recertification

All investigators and members of their research teams must meet University continuing education requirement every three (3) years after certification of initial education for as long as they are involved in human subject research. There is no exception to this requirement. Acceptable training includes:

- The University required CITI Refresher Modules (chosen in accordance with the criteria referenced above in Section 12.4.1.1), with a passing score on the required quizzes with a score of 80 or better

Or

- A refresher course in human research protections offered by ORC (available for groups of twenty or more trainees). This option also requires completion of modified CITI refresher course for the purposes of assessing competency with the course material, via a score of 80 or better on the required quizzes.

And

- Thorough review of all HRPP Updates/Reminders/Guidance/Hot Topics sent regularly by e-mail to the campus community from the ORC, or via the Vice President for Research's quarterly 'Research News', and/or
- Attendance at PRIM&R or OHRP seminars, conferences and webinars, and/or attendance at an ORC sponsored workshop, and/or
- Required training for investigators who are also IRB Chair, IRB members, or ORC staff (described in this policy under Section 2.13).

12.4.4 Additional Resources

Human research protection information will be made available on the ORC website, and via the IRB updates referenced above, on an ongoing basis to ensure that the University research community is apprised of current regulatory and policy requirements and training opportunities.

12.5 Investigator Concerns

Investigators who have concerns or suggestions regarding the University's human research protection program should convey them to the AVP-RC, the IO, or other responsible parties (e.g. college dean, departmental chair) regarding the issue, when appropriate. The AVP-RC will research the issue, and when deemed necessary, convene the parties involved to form a response for the investigator or make necessary procedural or policy modifications, as warranted. In addition, the IRB Chair, AVP-RC, or the IO will be available to address investigators' questions, concerns and suggestions.

12.6 Investigator Disclosures of Significant Financial Interest

The responsibilities and obligations of investigators to the University must be clearly separated from personal financial interests or other obligations. Prudent stewardship of public funds requires protecting University research, education and public service from being compromised by the private interests or obligations of any investigator.

Investigators will follow these SOPs located at Section 14, which set forth requirements and guidelines for:

- Disclosure of outside interests by investigators at the University who engage in University activities funded by specified internal and external entities;

- Review of investigator disclosures by University officials; and
- Identifying, reporting and managing conflicts of interest.

13 Sponsored Research

13.1 Policy

It is University policy that any sponsored research conducted under the auspices of the University is conducted in accordance with federal guidelines and ethical standards.

The following describe the procedures required to ensure that all sponsored research meets this requirement.

13.2 Definitions

Sponsor: The company, institution, individual donor, or organization responsible for the initiation, management or financing of a research study.

Sponsored research: Research funded by external entities through a grant or contract that involves a specified statement of work (e.g. the research proposal) with a related transfer of value to the sponsor, including clinical trials involving investigational drugs, devices or biologics.

13.3 Responsibility

All sponsor contracts for research involving human subjects are reviewed by the Office of Sponsored Programs (OSP). The Office of Research Compliance and OSP will share contract and study information as necessary for each sponsored protocol to ensure that the protocol, consent, and contract language are consistent. Additionally, OSP reviews sponsor contracts to ensure the following:

1. All sponsor contracts will indicate that the University will follow the protocol, applicable regulations and its ethical standards;
2. All sponsor contracts will define who will be responsible for research related injuries, where applicable (see section 13.4 below for University policy);
3. If the sponsor will monitor the conduct of the research, the contract will be required to state that if the study monitor uncovers information that could affect the safety of subjects or their willingness to continue participation, influence the conduct of the study, or alter the IRB's approval to continue the study, the sponsor will make sure that the information is communicated to the IRB;
4. If the sponsor discovers results that could affect the safety or medical care of subjects, the sponsor will make sure the IRB is notified;

5. When the sponsor is responsible for conducting data and safety monitoring, the agreement will require the sponsor to provide data and safety monitoring reports to the IRB and to report findings to the IRB that could affect the safety of subjects or influence the conduct of the research during or after the closure of the study and the timeframes for providing this information;
6. All sponsor contracts will contain provisions regarding the dissemination of research results including the right of the University investigator to publish results. The sponsor may retain the right to review prior to publication and in certain circumstances to delay publication for a reasonable time period; and
7. All sponsor contracts or other funding agreements require the sponsor to promptly (no longer than within thirty (30) days) report to the organization any findings that could affect the safety of subjects, influence the conduct of the study, or alter the IRB's approval to continue the study.

13.4 Policy on Payment of Research-related Injury Costs in Industry-funded and Initiated Clinical Trials

The University's role as a participating site in clinical trials that are funded and initiated by industry (e.g., pharmaceutical companies, device companies etc.) is critical in facilitating the evaluation and marketing of promising investigational (and new indications for approved) drugs, devices and biologics.

Given our patients' important contribution in assisting industry companies in their quest to market such test products for public good and financial gain, it is expected that costs associated with research-related injuries[1] occurring in SBU subjects volunteering in such trials must be borne by those companies. Subjects shall not be responsible, either directly or through their insurance, for payment of research-related injury costs in industry clinical trials.

This policy is not intended to waive any of a research subject's legal rights; or release the investigator, the sponsor, the University or its agents from liability for negligence.

Waivers of this policy will be considered on a case by case basis by the AVP-RC, the IO, and other University Officials as deemed necessary.

> [1]*Research-related injuries are those directly resulting from the test product or directly from properly performed study procedures. Such injury does not include normal progression of a subject's underlying disease, or injury resulting from interventions that would have been conducted whether or not the subject participated in the industry clinical trial.*

14 Conflict of Interest in Research

14.1 Policy

The responsibilities and obligations of Investigators to the University must be clearly separated from personal financial interests or other obligations. Prudent stewardship of public funds requires protecting University research, education and public service from being compromised by the private interests or obligations of any Investigator.
This policy sets forth requirements and guidelines for:

- Disclosure of outside interests by investigators at the University who engage in University activities funded by specified internal and external entities;
- Review of investigator disclosures by University officials; and
- Identifying, reporting and managing conflicts of interest.

14.2 Definitions

Conflict of Interest: When an Investigator or IRB member is, or may be, in a position to influence activities or decisions in the conduct of externally and applicable internally supported activities in ways that could lead to personal financial gain for the Investigator (and/or the Investigator's immediate family member), or give an improper advantage to third parties in their dealings with the University.

Conflicts of interest may also arise when Investigators or IRB members (and/or the Investigator's immediate family member) have outside obligations of any kind that are in substantial conflict with the Investigator's University responsibilities or the public interest.

Designated Institutional Official (DIO): The DIO is responsible for soliciting and reviewing Certifications from Investigators and developing Management Plans that specify the actions that have been and shall be taken to manage the Financial Conflict of Interest or Significant Obligation. The Vice President for Research (VPR) appoints the DIO and serves as the final arbiter in the appeals process.

Financial Conflict of Interest (FCOI): A Significant Financial Interest (SFI) that is related to, and that could (or could be perceived to) directly and significantly affect, the design, conduct, or reporting of externally and applicable- internally supported activities. The DIO makes the determination that an SFI constitutes a FCOI. When the activity involves human subjects, per OHRP and/or FDA as applicable, the IRB will also make an independent decision regarding the presence of a FCOI.

Financial Interest:

1. Any remuneration to the Investigator (and/or those of the Investigator's immediate family member) from outside the University, and/or

2. Any equity holdings or ownership of the Investigator (and/or those of the Investigator's immediate family member – spouse and dependent children), and/or
3. Intellectual property rights and interests (e.g., new technology disclosures, patents, copyrights) where a company has entered into an option to license, or license, such rights and interests from the University.
4. Intellectual property rights and interests upon receipt of income related to such rights and interests.

Note: All royalties, including those received by the Investigator from this University, are to be disclosed.

Financial Interest Related to the Research:
Financial interest in the sponsor, product or service being tested.

Financial Interest (FI) Exclusions:
- Income from investment vehicles, such as mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these vehicles;
- Income from seminars, lectures or teaching engagements sponsored by a federal, state or local government agency, a (United States) institution of higher education as defined at 20 U.S.C. 1001 (a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an institution of higher education; or
- Income from service on advisory committees or review panels for a federal, state or a local government agency, a (United States) institution of higher education as defined at 20 U.S.C. 1001 (a), an academic teaching hospital, a medical center, or a research institute that is affiliated with an institution of higher education.

Institutional Responsibilities: All professional responsibilities and activities for which the investigator was hired to perform at, and is paid by, this University, including but not limited to research, research consultation, teaching, professional practice, institutional committee memberships, and service on panels such as Institutional Review Boards or Data and Safety Monitoring Boards.

Investigator (specific to IRB submissions only): All study team members listed in the electronic management system for a project submitted to the IRB. For the purposes of this policy, "investigator" shall include the investigator's spouse and all dependent children.

Obligation: An unpaid position - held as an officer, trustee, director, adjunct professor, advisor, scientific advisor, board member or consultant of a for-profit or not-for-profit entity.

Significant Financial Interest (SFI): One or more of the following types of Financial Interests of the Investigator (and/or those of the Investigator's immediate family member) ***that reasonably appears to be related to the Investigator's Institutional Responsibilities*** is considered an SFI:

Publicly Traded Entity: Value of any remuneration received from the entity in the twelve months preceding the disclosure and/or the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000.

Non-Publicly Traded Entity**:** Value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds $5,000, and/or the Investigator (and/or the Investigator's Immediate Family Member) holds any equity interest.

Intellectual Property: rights and interests (e.g., patents, copyrights), royalties from such rights, and agreements to share in royalties related to such rights (upon receipt of income related to such rights and interests). At SBU, all royalties are to be disclosed, including those received by the investigator from this University.

Travel (PHS/NIH only): Investigators also must disclose the occurrence (over the preceding 12 months) of reimbursed travel or sponsored travel (i.e., that which is paid on behalf of the Investigator) that is related to their Institutional Responsibilities and which totals > $5,000 per reimbursing / paying entity. The disclosure must include the sponsor, destination, duration, and purpose of the travel. Excluded from this requirement is travel that is reimbursed or sponsored by federal, state or local government agency, an institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, a medical center or a research institute that is affiliated with an Institution of higher education.

Significant Obligations (SO): Significant Obligations (SO) includes obligations that would reasonably appear to be related to an investigator's institutional responsibilities.

14.3 Procedures for Financial Disclosure

Where the research activity involves human subjects, the DIO and the IRB retain responsibility for reviewing investigator financial disclosure and for promulgating conflict management plans. The IRB staff liaises with the DIO. The AVP-RC also serves as a non-voting ex-officio member of the COI Committee.

University Policy P209 (Investigator Conflict of Interest Policy) is followed regarding requirements for certification submissions, review, determinations of when significant financial interests and/or significant obligations constitute conflicts of interest, the development of conflict management plans, and reporting requirements.

In any such case where human subjects research is involved, the QA Administrator in the ORC notifies the DIO of all funded studies submitted to the IRB, and the DIO advises if any named investigator on the submission has an SFI or SO. These cases are brought to the full committee for review of conflict and management plan (if required) to ensure the protection of human subjects.

If any of the Investigators on the protocol have an FCOI or SO the IRB requires (where it is determined that the conflict can, in fact, be managed) that:

- The DIO provides written confirmation that the conflict of interest can be managed, and provides a proposed management plan. The IRB will review the plan, and may modify and/or add to it, as below. Where there is discrepancy or disagreement, the IRB's decision will supersede that of the DIO.
- The Investigator cannot be involved in the recruitment or consenting of subjects, and disclosure of such must be provided in the consent documents. If she/he is named in the consent form as not involved in recruitment or consenting of subjects, it means that the discussion of any details concerning the research protocol in question must be conducted by an IRB approved co-investigator. In the case where the investigator may be a patient's treating physician, she/he may state that there are standard therapies available, as well as research studies that the patient may be interested in hearing about. If the patient is interested in hearing more about his/her research options, referral to the IRB approved co-investigator must occur.

- The Investigator cannot place undue pressure on, or offer incentives to, other investigators to enroll subjects.
- A section of the consent form must be added that:

    - Is titled 'Notice of Investigator Conflict of Interest';
    - names the investigator(s) with the FCOI or SO;
    - describes, in lay language, the nature of the FCOI or SO;
    - states that the named investigator(s) will not be involved in recruitment or consenting of subjects ;
    - describes any other aspects of a management plan as required by the IRB.
- As with any study, the consent processes for any or all subjects may be witnessed by an IRB or ORC representative.

For clinical studies involving the use of investigational human drugs and biological products or medical devices, certifications and disclosure requirements are defined in Food and Drug Administration (FDA) regulations, Title 21 CFR Part 54.

14.4 Institutional Conflict of Interest

As an organization that conducts and reviews research involving human subjects, the University recognizes its obligation to protect the rights and welfare of those subjects, and ensure the integrity of the research and the human research protection program. Toward this end, the financial interests of the University or senior administrative officials at the campus/central levels must be identified, evaluated, managed, and minimized or eliminated in order to ensure that meeting that obligation is not jeopardized.

14.4.1 Definition of Institutional Financial Conflicts of Interest

An "**Institutional Financial Conflict of Interest"** arises in human subjects' research when a financial interest of SBU may affect or appear to affect the design, conduct, reporting, review, or oversight of the human subjects' research. Institutional financial conflicts of interest are of significant concern when they create the potential for inappropriate influence over a human subjects' research project, particularly to the integrity of the research and the safety and care of subjects enrolled in the research. All forms of potential Institutional Financial Conflicts of Interest in human subjects' research require disclosure, evaluation, and either management or elimination under this Policy.

An "**Institutional Financial Conflict of Interest"** (IFCOI) exists when:

1. The University receives or might reasonably be expected to receive royalty income from the sale of a product covered by any patent, license or copyright, whether issued or pending, held by SUNY/RF **and** is proposed to be used in human subjects' research projects at SBU;
2. The University holds or proposes to hold, directly or indirectly, any equity interests of any amount (or entitlement to the same), in research sponsors of human subjects' research projects, whether such research sponsor is public or non-public, through its technology licensing activities or investments related to such activities;
3. The University has received substantial gifts (including gifts in kind) from a potential commercial sponsor of human subject research or a company that owns or controls products being studied or tested in human subject research; and/or
4. Senior Administrative Officials with direct responsibility for human subject research (or their spouse, dependent children), as defined in Section II below:

    a. Holds a position such as an officer, trustee, director, employee or consultant in commercial research sponsors, or **any** company that owns or controls products being studied or tested in human subjects
    b. Receives remuneration from commercial research sponsors, or **any** company that owns or controls products being studied or tested in human subjects. **Remuneration**

includes salary and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship);

c. Holds any equity interest (e.g., stock, stock option, or other ownership interest) in commercial research sponsors, or **any** company that owns or controls products being studied or tested in a human subject
d. Holds intellectual property rights and interests (e.g., patents, copyrights), royalties from such rights, etc. relating to products being studied or tested in a human subject

14.4.2 Reporting

The following offices report at least semi-annually to the QA Administrator within ORC on interests described above:

1. Office of Intellectual Property Partners:
   - to report licensing arrangements, patents, invention disclosures;
2. Advancement Office/Stony Brook Foundation
   - to report gifts

The following institutional officials are considered senior administrative officials and must provide initial disclosure of their significant financial interests relating to human research and then receive reminders on an annual basis that if details have changed a new disclosure form needs to be submitted and reviewed for ICOI, with resulting management plans:

- President
- Provost
- Vice Presidents
- Deans
- Chairs (of departments identified by Office of Research Compliance [ORC] as conducting human research activities)

14.4.3 Review and Evaluation

IRB proposals submitted to the Office of Research Compliance in advance of IRB review and approval will be assessed by the QA Administrator for potential IFCOI by assessing applicability of information contained within the reports and forms referred to above.

As a matter of policy, the University will not participate in a human subject research project when it has an IFCOI. An exception to this policy may be made only when the Institutional Review Board, in consultation as deemed necessary with the COI Administrator, and/or Conflict of Interest Committee (as identified in University Policy P209) determines that:

- Circumstances exist to justify SBU's participation in the project while still maintaining the protection of human subjects, and
- A conflict management plan is adopted to maintain research integrity and serve the best interests of subjects enrolled in the research.

These circumstances and conflict management plans will be documented.

14.4.4 Conflict Management Plan

If the University's participation in a project is permitted notwithstanding the IFCOI, the University's participation will be subject to a conflict management plan developed and approved by the IRB as above. In the case of senior administrative officials, the conflict management plan shall be agreed to by the conflicted individual. The IRB has the final authority to determine whether any IFCOI and its management allows the research to be approved.

Options for managing institutional conflict of interest, include but are not limited to the following:

- Disclosing the institutional conflict of interest to research subjects in the consent process and documents.
- Disclosing the institutional conflict of interest to any journals or other publications for which the results of the research will be submitted.
- Recusing conflicted senior administrative officials from scientific merit review of human research
- Having an external, independent IRB review the research in question
- Monitoring of research by independent reviewers
- Divestiture of financial conflicts of interests
- Severance of relationships that create actual or potential conflicts.
- Prohibiting the conduct of the research at the University

14.4.5 Timing

The review, evaluation, and where applicable, management of an IFCOI shall be completed prior to the account establishment of an award for the human subject research project or beginning of the project (including enrollment of any research subject), whichever comes first. The study will remain unapproved, pending approval by IRB of the conflict management plan.

14.5 Investigator Conflict of Interest Unrelated to Current Financial Conflict of Interest

There are instances where a member of the study team has a vested personal interest in the future commercial success of the drug, device, etc. under study (e.g., was involved in discovery,

patent, licensing, IND/IDE filings etc.), but does not, at this time, have a significant financial interest that would trigger a review for FCOI, as defined above. In this situation, although recruiting or consenting of potential subjects by the affected Investigator is acceptable, a section should be added to the consent form that reads:

"Investigator's Personal Interest in this Study"
Dr. _____, who is one of the investigators conducting this study has a personal commercial interest in, or may financially benefit in the future from, the development of the [drug, device, etc.] being tested in this study.

14.4.6 Education

- Required every 4 years

- Education is required immediately when:
- Financial conflict of interest policies are revised in a manner that changes research requirements
- A researcher is new to the organization
- A researcher is non-compliant with financial conflict of interest policies and procedures

15 Subject Outreach

15.1 Policy

The University is committed to ensuring that educational opportunities are offered to research subjects, prospective research subjects, and community members which will enhance their understanding of activities involving human participation in research at SBU.

15.2 Research Subject Advocate (RSA)

The commitment of the Institution to our future and current research subjects is evident in the establishment of an ORC IRB staff member to serve as the Institution's Research Subject Advocate (RSA). This individual will:

- Work within University Hospital to promote educational efforts for patients regarding participation in research, and assist with, and streamline, procedures relating to recruitment of patients into research studies.
- Assist patients with navigating the research informed consent process.
- Disseminate materials, and organize educational events to train research volunteers, investigators, and staff regarding participant rights and protections.

- Serve as institutional liaison for ResearchMatch, the national recruitment registry that matches researchers to individuals who are interested in participating in research. (see Section 17.13 for more details on process)

15.3 Outreach Resources and Educational Materials

The RSA efforts include revising and augmenting a section of the Human Research website dedicated to informative outreach resources, now entitled "Volunteering in Research". This area on the website includes an overview of what it means to be a volunteer in research, and addresses Frequently Asked Questions (FAQs), as well as Institutional, and other relevant source brochures. The website provides several relevant links to the Office for Human Research Protections (OHRP) to inform the general public about research participation. Direct research-related links are provided to increase public awareness and educate the surrounding community regarding the importance of research, as well as the importance of their role in scientific advances.

The RSA participates in outreach activities (e.g., presence at health fairs, at University Hospital etc.) for community education efforts.

15.4 Evaluation

The RSA periodically evaluates outreach activities and revises efforts as deemed appropriate. These evaluations take place in an informal, ongoing manner. One such assessment of effectiveness is done via review of hits to the above-referenced website after various initiatives. RSA documents these assessments and revisions to the outreach program, and periodically meets with the AVP-RC to provide an update on the outreach program effectiveness and to address proposed activities and required resources moving forward.

16 Health Insurance Portability and Accountability Act (HIPAA)

16.1 Policy

Protected Health Information obtained by the University may not be used internally or disclosed to any outside person or organization for research purposes without prior approval of the IRB, and any other applicable HIPAA privacy and security policies in place at the University resulting from our University's status as a 'hybrid' covered entity.

The following describe the procedures for conducting research at the University in accordance with the Health Insurance Portability and Accountability Act (HIPAA) of 1996.

16.2 Definitions

Access: The mechanism of obtaining or using information electronically, on paper, or other medium for the purpose of performing an official function.

Authorization: A detailed document that gives covered entities permission to use protected health information for specified purposes, which are generally other than treatment, payment, or health care operations, or to disclose protected health information to a third party specified by the individual.

Covered entity: The term applied to institutions that must comply with the Privacy Rule. These include:

- Health plans
- Health care clearinghouses
- Health care providers who conduct certain financial and administrative transactions electronically. These electronic transactions are those for which standards have been adopted by the Secretary under HIPAA, such as electronic billing and fund transfers.

Common Rule: A federal policy on human subject protection that provides for the primary source of regulation of research.

De-Identified Information: Health information that does not identify an individual. In other words, there is no reasonable basis to believe that the information can be used to identify an individual. If information is de-identified it no longer is subject to the Privacy Rule and is exempt from HIPAA requirements.

Deletion: The removal, erasing, or expunging information or data from a record.

Disclosure: The release, transfer, provision of access to, or divulging in any other manner information outside of the covered entity.

Health Information. Any information created or received by a health care provider or health plan that relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or payment for the provision of health care to an individual.

Individually Identifiable Health Information (IIHI): A subset of health information, including demographic information collected from an individual that identifies the individual (either directly, or through codes/identifiers).

Limited Data Set: Protected health information that excludes specific direct identifiers of the individual or of relatives, employees or household members of an individual. A limited data set can only be used for the purposes of research, public health, or healthcare operations, and disclosed for the purpose of research.

Minimum Necessary: The principle that any access should be limited to the minimum amount of information needed to accomplish the intended purpose of the use or disclosure.

Privacy Board: The term used to describe a board comprised of members of varying backgrounds and appropriate professional competencies, as necessary, to review individual's private rights. The IRB is the University's privacy board.

Privacy Act: An act that provides for the confidentiality of individually identified and retrieved information about living individuals that is maintained in a system of records and permits the disclosure of records only when specifically authorized by the statute. The Act provides that the collection of information about individuals is limited to that which is legally authorized, relevant, and necessary.

Privacy Rule: Provides guidance on the use of protected health information in the conduct of research. It imposes requirements on those involved in research, both individuals and institutions. Privacy refers to a person's desire to control the access of others to themselves. The evaluation of privacy involves consideration of how the investigator will access information from or about subjects. The IRB members should use strategies to protect privacy interests relating to contact with potential subjects, and access to private information.

Protected Health Information: Individually identifiable health information transmitted or maintained electronically or in any other form or medium, except for education records or employment records, as excluded in the Privacy Rule.

Preparatory Research: The method applied to developing or designing a research study.

Waiver of Authorization: A means of requesting approval from the IRB (as the Privacy Board) rather than asking each research subject for an authorization to access protected health information.

16.3 Historical Background

The *Health Insurance Portability and Accountability Act of 1996* (HIPAA) required the creation of a Privacy Rule for identifiable health information. While the main impact of the Privacy Rule is on the routine provision of and billing for health care, the Rule also affects the conduct and oversight

of research. Investigators, IRB staff and IRB members, as well as research administration, must be aware of this information.

16.4 Research under HIPAA

HIPAA defines research as "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge." This definition is identical with the one used in the “Common Rule.”

16.4.1 Effects of HIPAA on Research

The Privacy Rule does not make any changes to the Common Rule. However, it does contain several provisions that resemble provisions of the Common Rule and does make reference to those provisions.

The University is a hybrid covered entity under HIPAA because it consists of components that are (e.g. health care providers in the University Hospital) and components that are not (e.g. academic departments in the College of Arts and Sciences, etc.) considered covered entities under HIPAA.

- Where the investigator is also a covered entity, i.e. a health care provider, then she/he is legally mandated to comply with all provisions of HIPAA when accessing or generating PHI.
- Where the investigator is not a covered entity (i.e. not a health care provider), the University requires that HIPAA procedures be followed as ‘best practices’, as described in this document.

In general, the Privacy Rule permits covered entities to use or disclose protected health information for research purposes when the individual who is the subject of the information authorizes the use or disclosure (exceptions are addressed below). Where authorization is required, the IRB uses a combined authorization/informed consent form which should be completed by the investigator and submitted to the IRB for review and approval.

16.4.2 Review Preparatory to Research

The Privacy Rule permits a covered entity to use or disclose protected health information to an investigator without authorization or waiver for the limited purpose of a “review preparatory to research.” Such reviews may be used to prepare a research protocol, or to determine whether a research site has a sufficient population of potential research subjects. Requests for a “review preparatory to research” must receive prior approval from the HIPAA Privacy Officer. The Institutional Review Board does not need to review this request.

16.4.3 Use and/or Disclosure of De-identified Health Information: NOT subject to HIPAA

Where the investigator proposes use of PHI from which the following 18 identifiers are removed, HIPAA does not apply to the research:

- Name,
- Address (street address, city, county, zip code -with certain exceptions),
- Dates (e.g. birth date, admission date, discharge date, date of death) and individual ages if over 89,
- Telephone numbers,
- Fax numbers,
- Electronic mail addresses,
- Social security numbers,
- Medical record numbers,
- Health plan beneficiary numbers,
- Account numbers,
- Certificate/license numbers,
- Vin and serial numbers, license plate numbers
- Device identifiers and serial numbers,
- Web Universal Resource Locators (URL's),
- Internet Protocol (IP) address numbers,
- Biometric identifiers (including finger and voice prints),
- Full face photographic images and any comparable images, and
- Any other unique identifying number, characteristic, or code.

Although HIPAA is not applicable, the IRB (as the IRB, not the privacy board) approval must be obtained before the proposed activity begins. A HIPAA De-Identification Form must be submitted along with the standard IRB submission paperwork.

16.4.4 Research on Protected Health Information of Decedents

The protections of the Common Rule apply only to living human beings; by contrast, the Privacy Rule also protects the identifiable health information of deceased persons (“decedents”). The Privacy Rule contains an exception to the authorization requirement for research that involves the protected health information of decedents. A covered entity may use or disclose decedents’ protected health information for research if the entity obtains representations from the investigator that the use or disclosure being sought is solely for research on the protected health information of decedents, that the protected health information being sought is necessary for the research, and, at the request of the covered entity, documentation of the death of the individuals

about whom information is being sought. Investigators should submit the HIPAA Research on Decedent PHI Form for IRB review and approval when they intend to conduct research involving decedents' protected health information.

16.4.5 Limited Data Sets with a Data Use Agreement

When an investigator requires certain data elements that are otherwise not permitted in de-identified data, as above, the Privacy Rule permits disclosure of a "Limited Data Set" to the investigator without obtaining patient authorization, provided that the investigator has signed a Data Use Agreement. The limited data set is still considered to be protected health information, but cannot include any of the following 16 identifiers:

- Names,
- Postal address info. (if other than city, state and zip),
- Telephone numbers,
- fax numbers,
- Email addresses,
- Social Security numbers,
- Medical record numbers,
- Health plan beneficiary numbers,
- Account numbers,
- Certificate/license numbers,
- Vin and serial numbers, license plate numbers,
- Device identifiers, serial numbers,
- Web URLs,
- IP address numbers,
- Biometric identifiers (finger prints), or
- Full face, comparable photo images.

The Privacy Rule requires that the Data Use Agreement used in conjunction with the Limited Data Set contain provisions that:

1. Establish the permitted uses and disclosures of the Limited Data Set by the recipient, consistent with the purposes of the research, and which may not include any use or disclosure that would violate the Rule if done by the covered entity;
2. Limit who can use or receive the data; and
3. Require the recipient to agree to the following:
    a. Not to use or disclose the information other than as permitted by the data use agreement or as otherwise required by law;

b. Use appropriate safeguards to prevent the use or disclosure of the information other than as provided for in the data use agreement;
c. Report to the covered entity any use or disclosure of the information not provided for by the data use agreement of which the recipient becomes aware; ensure that any agents, including a subcontractor, to whom the recipient provides the Limited Data Set agrees to the same restrictions and conditions that apply to the recipient with respect to the Limited Data Set; and
d. Not to identify the information or contact the individual.

Investigators who will be receiving a Limited Data Set must submit a signed copy of the covered entity's Data Use Agreement to the IRB for approval, prior to initiating the research.

16.4.6 Waiver of Authorization for Use or Disclosure of Protected Health Information in Research

Under the Privacy Rule, covered entities are permitted to use and disclose protected health information for research with individual authorization, or without individual authorization under limited circumstances. A covered entity may use or disclose protected health information for research without individual authorization, when presented with documentation that the IRB has granted a waiver of authorization [see 45 CFR 164.512(i)(1)(i)]. This provision of the Privacy Rule might be used, for example, to conduct records research, epidemiological studies, or other research where de-identified data is unavailable or not suited to the research purpose.

The waiver documentation presented to the covered entity must include the following:
1. Identification of the IRB and the date on which the alteration or waiver of authorization was approved;
2. A statement that the IRB has determined that the alteration or waiver of authorization, in whole or in part, satisfies the three criteria in the Rule;
3. A brief description of the protected health information for which use or access has been determined to be necessary by the IRB;
4. A statement that the alteration or waiver of authorization has been reviewed and approved under either normal or expedited review procedures; and
5. The e-signature of the IRB Chair or other IRB member, as designated by the IRB Chair.

The following criteria must be satisfied for the IRB to approve a waiver of authorization under the Privacy Rule:

Note: *The use or disclosure of protected health information involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:*
1. An adequate plan to protect the identifiers from improper use and disclosure;

2. An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law;
3. Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by this subpart;
4. The research could not practicably be conducted without the waiver or alteration; and
5. The research could not practicably be conducted without access to and use of the protected health information.

Patient Rights and Research

Under HIPAA, patients have certain rights. Those that may affect research include the right to receive a Notice of Privacy Practices, the right to access, inspect, and receive a copy of one's own PHI, the right to request an amendment to one's own PHI, and the right to an accounting of certain disclosures of PHI that occur outside the scope of treatment, payment and health care operations that have not been authorized.

16.5 HIPAA and Documentation Requirements

Where health information is proposed for use or disclosure in a research activity, applicable HIPAA documents must be included with the IRB submission, e.g.:

- Consent/authorization form,
- HIPAA Waiver of Authorization Form,
- HIPAA Limited Data Set Form,
- HIPAA Research on Decedents Form,
- HIPAA Preparatory to Research Form, or
- HIPAA Deidentification Form

For investigators using University Hospital facilities and/or patients, the '**Application for Approval to Conduct Research Activities at Stony Brook University Hospital Inpatient or Outpatient Facilities'** (available in the electronic management system's forms library) must be uploaded, and the HIPAA Privacy Officer must e-certify to approve data disclosure to the study sponsor.

17 Special Topics

17.1 Quality Assurance/ Quality Improvement (QA/QI) Activities vs. Research Activities

QA/QI initiatives are a mandated function of the University Hospital. Some of these initiatives are implemented after thorough evidenced-based best practices are identified, in response to an identified safety issue, or to improve the delivery of care and avoid potential safety issues. **The overarching intent of the initiatives is continuous monitoring of hospital operations and improved care of our patients at Stony Brook University Medical Center.**

Please note that the 'Application for Designation of Activity as Quality Assurance/Quality Improvement or Research" is available in the electronic management system in the Forms and Documents Library to assist the investigator in the proper designation for the activity.

QA/QI initiatives

The following activities are not considered research activities at the University. The responsible conduct of the activities listed below falls under the jurisdiction of SBUMC's Division of Medical and Regulatory Affairs and/or a hospital-recognized departmental quality assurance committee (collectively referred to from this point on as 'Hospital QA'):

- Any hospital QA initiatives, and presentation/publication of results thereof, that are conducted within SBUMC only, and that serve to:
  - Measure or improve SBU's ability to meet or exceed an existing national standard of care or benchmark (Joint Commission, etc.), OR
  - **Develop** a standard of care or benchmark **for applicability within SBUMC.**
  - **Submission of data to a national or state registry/database:**
    - That is mandated at the state or federal level, OR
    - That directly impacts reimbursements and funding available from the state, Department of Health, or federal Centers for Medicare & Medicaid Services (CMS) based on performance and/or clinical or quality outcomes, OR
    - That is maintained by an organization/consortium, formally recognized by SBUMC's Division of Medical and Regulatory Affairs, **the principal purpose of which is** benchmarking and/or performance improvement, the use of which is for internal University activities.

- Hospital QA use of data from a registry/database, meeting any of the criteria above, for the purpose of:
  - **Measuring or improving SBU's** ability to meet or exceed an existing national standard of care or benchmark (JCAHO, etc.). OR
  - **Developing** a standard of care or benchmark **for applicability within SBUMC.**

17.1.1 Research Activities

The following activities are considered research activities. The responsible conduct of the activities below fall under the jurisdiction of ORC and/or Institutional Review Board (IRB):

- Any hospital QA initiative, conducted within SBUMC only, designed to **develop** a standard of care or benchmark **for general applicability** (i.e. not only for operations within SBUMC, but to outside entities as well).
- Any QA or QI initiatives (including those proposing to **develop** an operational standard of care or benchmark) that are "investigator-initiated", i.e., that have not been vetted through, and endorsed by, SBUMC's Division of Medical and Regulatory Affairs and/or a hospital-recognized departmental QA committee).
- Submission of data to a registry/database that is not covered by those described above.
- Use of data from any registry/database for the purpose of measuring, improving or developing a standard or benchmark, under any condition not covered in the section above, including the use of registry data for the purpose of research.
- Any activity that proposes comparisons of one or more prospective interventions that are deliberately administered or made available (through a randomization or other process) to some patients (if within the University) or some hospitals (if part of a consortium or organizational effort) and not to others. This does not include, e.g. initiating a QI process in a small percentage of patients at SBUMC first to ensure feasibility, before introducing it to the entire patient population.

17.1.2 Activities that have a mix of both QA/QI and Research Components

Where your activity involves a mix of activities from Sections A and B, you will need to ensure compliance with the applicable entity, i.e. SBUMC's Division of Medical and Regulatory Affairs for the QA/QI aspects and ORC IRB for the research aspects of the activity (including securing approval prior to conducting the research aspect).

For any 'questionable' (QA vs. Research) activity not described above, please consult with the ORC and/or the Division of Medical and Regulatory Affairs for assistance.

17.2 Data/ Tissue Registries/ Banks

17.2.1 Mandated Registries and Biobanks

Mandated registries and biobanks are those:

- That are required by a state or federal agency, or

- That directly impact reimbursement and funding available from the state, Department of Health, or federal Centers for Medicare & Medicaid Services (CMS) based on performance and/or clinical or quality outcomes, or
- That are required to meet Joint Commission and other written standards for the treatment, payment, and/or operation of SBU's University Hospital (SBUH), SBUH departments or SBU Clinical Practice Management Plan (CPMP).

These activities are not under IRB jurisdiction. However, proposed research on identifiable data or specimens from such registries or biobanks would require prior review and approval or exemption by an SBU IRB.

17.2.2 Non-Mandated Registries and Biobanks:

Non-mandated registries and biobanks are those that are not listed above as mandatory. IRB oversight is dependent on the intent of the registry or biobank.

If the primary intent of the registry/biobank is for SBU-recognized quality assurance activities, then the creation of the registry/biobank does not fall under the jurisdiction of the IRB. The creation, and subsequent QA use of data or tissue from, the registry or biobank, must not begin without prior written approval by an appropriate authority (see Section 17.1 for additional guidance on QA activities at the University).

Any intent of the registry or biobank to bank data or tissue for future use in research activities requires IRB approval. Institutional Review Board approval is required for the creation of the registry or biobank, and IRB review and approval (or exemption) is required for the individual research activities that use the banked data or tissue. This includes:

- Informed Consent: Patients must consent to their data and/or tissue being banked in a non-mandated registry/biobank. Their consent is for the banking process only, and the consent process must be clear that each subsequent research use of the patient's (now subject's) data or tissue will undergo an ethics review to determine ethical and scientific merits of the proposed research.

- HIPAA Authorization: Patients must provide HIPAA authorization for their data and/or tissue to be banked in a non-mandated, non-QA registry/biobank.

- Confidentiality: Certificates of Confidentiality

- (https://grants.nih.gov/grants/policy/coc/index.htm) should be obtained for each registry and biobank to protect the confidentiality of the stored data and tissues.

- The National Institutes of Health have indicated that they will not issue discretionary Certificates of Confidentiality for the establishment and maintenance of data/biospecimen repositories where the main original source of the data/biospecimens was for clinical care or commercial purposes, rather than research sources. NOTE: a Certicate of Confidentiality request for individual studies using data or biospeciments from the repository will be considered for a CoC.

- Licensure: Biobanks must operate under appropriate licensure from the NYS Department of Health; See section 17.2.3 below for more information.

17.2.3 Stony Brook University BioBank

Stony Brook University operates a licensed BioBank, currently under the oversight of Dr. Kenneth Shroyer, Chair of Pathology. Any biobank that is proposed must be specifically added to the University's license on file with the NYS Department of Health

17.3 International Research

The IRB will review all international research using human subjects to assure adequate provisions are in place to protect the rights and welfare of the subjects.

Approval of research is permitted if "the procedures prescribed by the foreign institution afford protections that are at least equivalent to those provided in 45 CFR 46."

All policies and procedures that are applied to research conducted domestically should be applied to research conducted in other countries, as appropriate.

For international research, the IRB seeks sufficient knowledge of the local research context by requesting approval for the project from local IRBs or ethics committees (which may or may not be OHRP-registered) and/or local letters of support. The source of this information will depend on the nature of the study, on the country and on the resources available to the PI. Where there is a local IRB/IEC, the IRB must receive and review the foreign institution or site's IRB/IEC review and approval of each study prior to the commencement of the research at the foreign institution or site.

In some circumstances where research may be performed internationally and/or in settings where there are no IRBs, the IRB may, prior to approval of the research, require additional verification

and information from people outside the particular research project who are familiar with the customs, practices, or standards of care where the research will be taking place, such as local IRBs or ethics committees, other investigators with knowledge of the region, or other experts with knowledge of the region. The AVP-RC, , will review all transnational research proposals to determine whether the IRB has the qualifications to review the proposed research, or requires expertise of a consultant. Use of consultants will be required when none of the investigators are from the international site and there is no local site/contact. These consultants may either provide a written review of a particular protocol or attend an IRB meeting to provide the IRB with recommendations based on his or her expertise.

For federally funded research, approval of research for foreign institutions or sites “engaged” in research is only permitted if the foreign institution or site holds an Assurance with OHRP and local IRB review and approval is obtained.

Approval of research for foreign institutions or sites “not engaged” in research is only permitted if one or more of the following circumstances exist:

- When the foreign institution or site has an established IRB/IEC, the Investigator must obtain approval to conduct the research at the "not engaged" site from the site’s IRB/IEC or provide documentation that the site’s IRB/IEC has determined that approval is not necessary for the Investigator to conduct the proposed research at the site.
- When the foreign institution or site does not have an established IRB/IEC, a letter of cooperation must be obtained demonstrating that the appropriate institutional or oversight officials are permitting the research to be conducted at the performance site.
- IRB approval to conduct research at the foreign institution or site is contingent upon receiving documentation of the performance site’s IRB/IEC determination, or letter of cooperation, as applicable.

17.3.1 Responsibilities

1. It is the responsibility of the University investigator and the foreign institution or site to assure that the resources and facilities are appropriate for the nature of the research.
2. It is the responsibility of the University investigator and the foreign institution or site to confirm the qualifications of the investigators and research staff for conducting research in that country(ies).
3. It is the responsibility of the University investigator and the foreign institution or site to ensure that the following activities will occur:
   a) Initial review, continuing review, and review of modifications;
   b) Post-approval monitoring;
   c) Handling of complaints, non-compliance and unanticipated problems involving risk to subjects or others; and

4. The IRB will not rely on a local ethics committee that does not have policies and procedures for the activities listed above.
5. It is the responsibility of the University investigator and the foreign institution or site to notify the IRB promptly if a change in research activities alters the performance site's engagement in the research (e.g., performance site "not engaged" begins consenting research subjects, etc.).

17.3.2 Consent Documents

The informed consent documents must be in a language understandable to the proposed subjects, with the credentials of the translator detailed in the IRB application or amendment form. Researchers and research staff must follow regulatory and IR requirements when using this method.

17.3.3 Monitoring of Approved International Research

The IRB is responsible for the ongoing review of international research conducted under its jurisdiction through the continuing review process in accordance with all applicable federal regulations.

When the IRB and a local ethics committee will both be involved in the review of research, the PI will be responsible for ensuring coordination and communication with the local IRB/IECs.

The PI will be required to review and confirm compliance with any cited provisions provided in the current International Compilation of Human Subject Research Protections available through OHRP at http://www.hhs.gov/ohrp/international/index.html . When the foreign institution or site does not have an established IRB, a letter of cooperation must be obtained demonstrating that the appropriate institutional or oversight officials are permitting the research to be conducted at the performance site.

17.4 Registration of Clinical Trials

This institution requires PIs of certain investigator-initiated clinical trials to comply with federal requirements concerning registration of their studies on www.clinicaltrials.gov, **no later than 21 days after enrollment of the first participant**, if their study is described by any of the following:

- Funded (wholly or in part) by NIH, and meets the NIH definition of a clinical trial, i.e.. In order to meet the NIH definition of a clinical trial, the answer to all four of the following questions is yes:
  - Does the study involve human participants?
  - Are the participants prospectively assigned to an intervention?

- Is the study designed to evaluate the effect of the intervention on the participants?
- Is the effect that will be evaluated a health-related biomedical or behavioral outcome?

- See https://grants.nih.gov/policy/clinical-trials/definition.htm for details.
- Not funded by NIH, and is (1) a clinical trial of drugs and/or biological products that is a controlled, clinical investigation, other than a Phase I investigation, of a product subject to FDA regulation (see https://clinicaltrials.gov/ct2/manage-recs/fdaaa);

- Not funded by NIH, and is a prospective clinical study of health outcomes comparing an intervention with a device product against a control in humans (other than a small feasibility study), or any pediatric post-market surveillance study, as required under the Federal Food, Drug and Cosmetic Act (see https://clinicaltrials.gov/ct2/manage-recs/fdaaa)

In addition, many ICMJE journals (http://www.icmje.org/) require clinicaltrials.gov registration in order to consider articles for publication. However, the ICMJE requires that the study meeting the ICMJE definition of a clinical trial for registration on a public trials registry. The ICMJE definition is as follows: "any research project that prospectively assigns people or a group of people to an intervention, with or without concurrent comparison or control groups, to study the relationship between a health-related intervention *and* a health outcome. Health-related interventions are those used to modify a biomedical or health-related outcome; examples include drugs, surgical procedures, devices, behavioral treatments, educational programs, dietary interventions, quality improvement interventions, and process-of-care changes. Health outcomes are any biomedical or health-related measures obtained in patients or participants, including pharmacokinetic measures and adverse events."

Contact the Office of Research Compliance for first-time access to the clinicaltrials.gov site.

17.5 Guidance on Research (only) Involving Coded Private Information or Biological Specimens

When dealing with the review of biological specimen use in research activities, the IRB must balance two factors: the need for protection of the rights and welfare of the person from whom the specimen was/will be obtained and the need to not impede the research activities conducted at Stony Brook University.

The reader should also review Section 17.2, which addresses research involving tissue registries/tissue banks.

Under the definition of human subject at 45 CFR 46.102(f), *obtaining* identifiable private information or identifiable specimens for research purposes constitutes human subject research. Obtaining identifiable private information or identifiable specimens includes, but is not limited to:

1. Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens that have been provided to investigators from any source; and
2. Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens that were already in the possession of the investigator.

In general, OHRP considers private information or specimens to be individually identifiable as defined at 45 CFR 46.102(f) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

Conversely, OHRP considers private information or specimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

For example, OHRP does not consider research involving only coded private information or specimens to involve human subjects as defined under 45 CFR 46.102(f) if the following conditions are both met:

1. The private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; **And**
2. The investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
    a) The investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (Note: the HHS regulations do not require the IRB to review and approve this agreement);
    b) There are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
    c) There are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

The IRB operates under the general rule that if an investigator **can** get consent from a prospective subject, than she/he **should** get consent from that subject. This is the case in most instances of research proposing prospective collection of biological specimens. Exceptions to this general requirement (e.g. in the case of future discarded surgical specimen, etc.) may be granted only if the consent waiver criteria are submitted, and deemed appropriate by the IRB.

For biological specimen research ask whether the activity will generate information that has known clinical significance for diagnosis or prediction of a disease state for either the subject or the subject's family members

If the answer is NO, the (non-physical) risks for the activity are deemed minimal, i.e. they are theoretical in that clinical significance *may* be determined in the future. The possible risk then becomes one of a breach of confidentiality and/or the subject not knowing that this significant, private information now exists.

Where consent is required by the IRB, possible consent language in the procedures section (where consent is required) includes:

> *"Results from testing of your tissue will not be understood unless we pool it together with data from other study subjects. Because this is research, the clinical significance (if any) of your individual results may not be understood for years. Therefore, individual test results will not be shared with you or your doctor."*

If the PI wishes to contact subjects if and when the clinical significance of the results becomes clear, possible consent language includes:

> *"If, in the future, findings from this study are confirmed by the scientific community and have definite implications for your health (or your children or future offspring), we will make a best effort to send you a letter describing the general results and offering ways to obtain care and/or counseling. If you initial here_____, it means you do not want to be contacted if future findings become relevant to you."*

If the answer is YES, the (non-physical) risks associated with the study are deemed more than minimal. These risks are as follows (and should be considered when drafting the foreseeable risks section of the consent document):

When subjects already have the disorder for which biological testing is being done: Risks may include possible breaches of confidentiality (affecting insurability, employability, etc.) and (where applicable) unintentionally uncovering unintended incidental genetic information (e.g. non-paternity, hereditary risks, risks of future diseases). Benefits could include confirmation of clinical diagnosis, where applicable, or else indicate clearly that no direct benefit exists for the subject.

When subjects are not yet known to have the disorder for which biological testing is done: Risks include those above, as well as (where applicable) psychological risks, determination of the possible presence of a heritable disorder (in themselves or their current/future offspring, accordingly). This research activity could also be of direct benefit, e.g. giving the subject the ability to inform family and to make appropriate lifestyle and reproductive choices; offering the potential for more effective intervention).

Further:

- If there are hereditary implications, genetic counseling by a genetic counselor or other qualified health care provider is required **prior** to participation in the study. Consent should indicate who will cover the cost of the counseling.
- There is an obligation to inform the subject of the test results in a timely manner after they are known. However, the subject should be offered an opt-out option (to not be told).
- Consent documents must indicate that the results of the research testing must not be used as the basis for clinical decision making, and the subject should seek confirmation of research test results in a certified clinical laboratory.

Information generated from specimen analysis

Another important aspect of specimen research to consider is that fact that the information that will be generated from analysis of the tissue will likely constitute 'health information', therefore requiring that the study be in compliance with privacy regulations, i.e. HIPAA. Section 16 must be reviewed to ensure that either:

- HIPAA authorization language is included in the Confidentiality/Privacy section of the subject consent document; OR
- One of three HIPAA forms is provided with the IRB submission so that the Investigator can attest to the fact that authorization from the subject is not required. Either:
  - A HIPAA De-identification Form, OR
  - A Limited Data Set Form, OR
  - A HIPAA Waiver of Authorization Form

17.5.1 General Issues to Consider in Biological Specimens Research

If the banking of biological specimens is proposed within the context of a larger (multi-center) research study, the following issues can be addressed within the main research consent form, but the actual request for consent to bank the tissue must be separated out from the request to consent for the main study. This can be achieved by adding yes/no statements (with a signature or initial lines) right before the signature lines of the main consent.

For example:

1. Do you agree to allow use of extra blood obtained from this study/extra tumor from your surgery for use in future research, the purposes of which are unknown at this time? If you agree, any future studies using your sample will be subject to further regulatory review.
2. Do you agree to allow someone to contact you in the future to ask you questions about your health or to ask you to participate in more research?

3. At the time of the proposed activity, is it the intent of the investigator or the company collaborator/sponsor to produce a commercially valuable product? If yes, disclose in the consent form whether or not the subject or his/her heirs will receive a portion of the profits. Note that consent forms cannot contain language through which the subject is made to waive, or appear to waive, any of his/her legal rights. An acceptable **example of consent language is:**

   "We may, in the future, be able to produce a commercially valuable product from the work done on samples collected from subjects in this study. It is not our intention to pay you or your heirs, for profits derived from such a product."

4. What happens to the specimen(s), and the data derived thereof, if the subject decides to withdraw from the study? Is the tissue removed from the study analysis or from the tissue bank? If so, state so in the consent. If it is not the intention to remove the sample or any data derived from it, state so in the consent. What about cell lines that have been generated?
5. How long will the biological specimen be kept? (It is acceptable to indicate, in the consent form, that the specimen will be kept for an indefinite amount of time).
6. If a new study proposes secondary use of biological specimens, i.e., use of samples collected for a previously conducted study, an assessment will be made by the IRB regarding whether or not the consent that was obtained for the first study is applicable to the second. If the purpose of the new study differs significantly from the purposes stated in the original study, and the specimens are identifiable, obtaining new consent will be required, unless the consent waiver criteria are met. The IRB therefore recommends obtaining the initial consent for research with as broad a stated purpose as possible such as, e.g. "the causes and treatments of lung cancer" etc..
7. Given the study aims and risks, should the investigator obtain a study-specific Certificate of Confidentiality from the NIH to protect against disclosure required by issuance of a subpoena. This is an extra protection for confidentiality if the study can potentially generate information that is particularly sensitive (e.g. HIV status, history of alcoholism, possible mental illness, etc.) For more information, visit: https://humansubjects.nih.gov/coc/index

17.6 Policy on Payment of Research Related Injury Costs Due in Industry-funded and initiated Clinical Trials

The IRB supports the University's role as a participating site in clinical trials that are funded and initiated by industry ('Industry Clinical Trials' e.g. pharmaceutical companies, device companies etc.). Such participation is critical in facilitating the evaluation and marketing of promising investigational (and new indications for approved) drugs, devices and biologics.

Given our subjects' important contribution in assisting industry companies in their quest to market such test products for public good and financial gain, it is expected that costs associated with research-related injuries* occurring in University subjects volunteering in such trials must be borne by those companies. Subjects shall not be responsible, either directly or through their insurance, for payment of research-related injury costs in industry clinical trials. Waivers of this policy will be considered on a case by case basis through consultation with the IO, Office of Sponsored Program (Clinical Trials Contracts division), and the AVP-RC as required.

This policy formalizes a long-standing procedural requirement of the IRB and is not intended to waive any of a research subject's legal rights; or release the investigator, the sponsor, the University or its agents from liability for negligence.

***Research-related injuries** are those directly resulting from the test product or directly from properly performed study procedures. Such injury does not include normal progression of a subject's underlying disease, or injury resulting from interventions that would have been conducted whether or not the subject participated in the industry clinical trial.

17.7 Application of ICH-Good Clinical Practice (GCP)

The IRB reviews research, and investigators conduct research in accordance with "Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance" when the sponsor funding the research requires such compliance, per citation in the study protocol. When this is the case:

The investigator will:

- Confirm compliance with these requirements, via review, completion, and uploading of the Supplemental Form D: ICH-GCP into the applicable electronic management system package.

The IRB will:

- Follow these standard operating procedures that are in compliance with sections 3.1-3.4 of the above document and additionally confirm, for the study in question:
  - All payments are prorated
  - Alternatives are provided with risks/benefits assessment
  - Costs and treatment in case of injury are clearly addressed
  - Subject responsibilities are addressed (distinct section)
  - Subjects will be given a SIGNED and DATED copy of the ICF

17.8 Policy on Non-English Speakers as Research Subjects

17.8.1 Inclusion of Non-English Speakers

Non-English speakers must be offered inclusion in studies where there is a potential for therapeutic benefit and no *reasonable* alternative or option is available outside of the research (i.e., in clinical care). For example:

- Many of the cooperative oncology group protocols would qualify in this category, i.e. testing experimental drugs that do not have a reasonable alternative in clinical care.
- Certain studies involving potentially therapeutic benefit via non- or less- invasive procedures where the only clinical alternative would be invasive

For these types of studies, the special protections addressed in sections 17.8.2 and 17.8.3 below would need to be adequately addressed as a condition of IRB approval.

For studies that do not qualify as cited above, investigators should remember that they must always develop eligibility criteria for their studies that consider safety, protection of vulnerable populations, and of course, the purpose of the research. Although not required as a condition of IRB approval (as it is above), all individuals meeting study eligibility criteria should be offered enrollment, regardless of the language they speak. Protections addressed below in sections 17.8.2 and 17.8.3 can be addressed on an expedited, 'as needed', basis, if and when the opportunity presents itself to discuss a study with a non-English speaker.

17.8.2 Consenting a Non-English Speaking Subject

Except as provided in section 5.8 of these SOPs, informed consent must be obtained, and it must be documented by the use of a written consent form approved by the IRB.

The person obtaining consent from a non-English speaking subject's consent should either be a study investigator who is fluent in English and the language of the subject, or a study investigator or team member (for minimal risk research) who is assisted by either a qualified interpreter (non-family member) or a recognized interpreter service.

Informed consent should be documented by the use of either:

A translated version of the IRB approved 'full' English consent form that embodies the basic and required additional elements of informed consent. An affidavit of accurate translation from the IRB approved English version must be provided from a qualified translator who is unaffiliated with the study. The translated consent form and affidavit must be submitted and approved by IRB

before its use. The document is signed and dated by the subject or the subject's legally authorized representative at the time of consent. A copy of the signed and dated consent form must be given to the person signing the form.

Or

A "short form" written consent document which states that the elements of informed consent have been presented orally to the subject or the subject's legally authorized representative. Researchers and research staff must follow regulatory and IR requirements when using this method. Both the short form and the oral presentation must be presented in the language of the subject. The IRB must receive and approve all foreign language versions of the short form document (along with translator affidavit) prior to use. Note that English and Spanish versions of an IRB acceptable 'short form' document are available in the forms library of the electronic management system.

When this 'short form' method is used:

1. The oral presentation should be conducted by either a study investigator who certifies to the IRB that she/he is fluent in English and the language of the subject, or a study investigator who is assisted by either a qualified translator unrelated to the study, or a recognized interpreter service, and
2. There must be a witness to the oral presentation who is fluent in both English and the language of the subject. Note:

- If an unaffiliated, qualified interpreter or service is used in the oral presentation as above, that individual may serve as the witness,
- a family member may not serve as the witness, and

3. The IRB must approve a written summary of what is to be read to the subject. Note: the IRB approved English consent form may serve as the summary, and
4. The witness must sign both the short form and a copy of the summary; and
5. The person actually obtaining consent must sign a copy of the summary; and
6. A copy of the summary must be given to the subject or representative, in addition to a copy of the short form.
7. In addition to receiving a copy of the (English) summary and a copy of the short form at the time of consenting, the subject must receive a copy of the summary, translated into their native language, as soon as possible after their enrollment into the study. The translated version of the consent form and the translation affidavit must be approved by the IRB prior to use.
8. The short form can only be used when all of the following conditions are met:

- There are possible benefits to the subject

- The study is a clinical trial
- There is FDA oversight for the study
- The study includes more than one visit so that the subject can be provided with the translated summary "consent form" at the upcoming visit.

17.8.3 Handling Visits and Procedures with a Non-English Speaking Subject

Investigators who are not fluent in the language spoken by the subject are expected to have a qualified interpreter present (or translation service used) for visits/procedures. This person cannot be a family member if the study is deemed greater than minimal risk to the subject.

17.9 SBU Guidance on the Management of Incidental Findings in Human Research

Note: This guidance borrows concepts (with permission) from Yale IRB Policy 720 (Incidental Findings with Possible Health and Safety Significance for Research Participants; https://your.yale.edu/policies-procedures/policies/720-irb-policy-720-incidental-findings-possible-health-and-safety) and the article 'Managing Incidental Findings in Human Subjects Research: Analysis and Recommendations', Wolf et. al. Journal of Law, Medicine and Ethics, Volume 36, Issue 2, pages 219–248, Summer 2008.

Unless specifically addressed otherwise, where the word subject is used in this document, it is meant to encompass adult subjects, minor subjects who assent for research, parents who give permission for those minor subjects, and legally authorized representatives of adult subjects who cannot consent for themselves.

17.9.1 Definition

Incidental Finding (IF):

A finding that:
- Concerns an individual research subject that has potential health or reproductive importance; and
- Is discovered in the course of screening for, conducting, or analyzing results from research; and
- Is beyond the aims of the study, i.e., occurring from variables not directly under study.

17.9.2 Background

Federal regulations [45 CFR 46.111(a)(6)] require that studies have adequate provisions for enrollment screening and data monitoring to ensure the safety of subjects. In the course of

carrying out these provisions, information that is secondary to the goals of the research may be identified which may impact the safety and/or wellbeing of the subjects.

These IF's have risks and benefits associated with them. For example, discovery of a possible abnormality during the course of a research-related fMRI study may lead to anxiety, as well as costs of further evaluation to determine clinical relevance (whether or not it ultimately turns out to be clinically relevant). However, an IF may also save a subject's life, if, e.g. that abnormality turns out to be an operable brain tumor. It is important, and respectful to the potential subjecs, to be clear in the consent process regarding the possibility of IFs, and procedures to be followed if they are uncovered. This information may impact a subject's willingness to participate in a given research study.

It is not the intent of this guidance to imply that investigators have an obligation to proactively search for IFs in research data/scans. It is important during the consent process to ensure that the subject understands that the goal of research is to collect data to answer the study aims, not to provide health information to individuals. It is also important not to foster a 'therapeutic misconception', i.e., that participation in a research activity will yield clinical benefit, or that the absence of an IF implies a 'clean bill of health'.

17.9.3 Procedures for IFs that are Reasonably Foreseeable

Certain types of research, e.g., research involving certain genetic/genomic analyses, or experimental scanning (MRI, CT, PET etc.), have a high potential for discovery of IF's. In developing these, and other types of research studies, Principal Investigators have an ethical obligation to subjects to assess the 'reasonably foreseeable' potential for IF's, identify and assess the types of IF's possible, and procedures to be followed for disclosure to subject.

The PI has primary, hands on, responsibility in this process. Members of the study team must be knowledgeable of the plan such that suspected IF's are reported to the PI for implementing the plan from that point forward.

17.9.4 Submission to the IRB

The submission to the IRB should include:

- **A summary of the assessment referenced above, i.e., a general description of the IF's that are possible in the activity,** along with incidence of occurrence (based on available literature). As examples, MRI's could uncover possible tumors or evidence of prior stroke; genetic analyses could uncover questions of paternity.

- Consideration should also be made regarding the need to re-contact the subject, if future analyses of data may uncover IF's after participation has ended.
- **The plan, if any, for assessing the significance of IF's, including involvement of outside consultants/experts to assist in said assessment**.
- This assessment is not for the purpose of determining whether or not to inform the subject, but for the purpose of gathering information to provide to the subject so that they can weigh for themselves the IF's associated 'risks' (e.g. anxiety, possible costs of follow-up) , 'benefits' (e.g. discovery of an operable tumor), and need for follow-up.
- Any involvement with outside individuals or departments should be in place prior to commencement of the activity (and associated costs, if anticipated, should be built into the budget). If applicable, these arrangements should be addressed in the consent process so that the subject can consent to their information being shared in this manner for IF assessment.
- **The process to be followed for disclosure to the subject:**

    - Depending on the types of potential IFs and/or potential clinically meaningful findings, disclosure to the subject may need to be conducted by a licensed physician (or psychologist, genetic counselor, or other professional as appropriate). If nonprofessional study personnel are to be responsible for conveying test results, they may want to consult beforehand with such professionals in order to be able to conduct an informative discussion with the subject. These details should be included in the plan submitted to the IRB.
    - The default for IF disclosure should be that such disclosure is made directly to the subject, consistent with respect for the subject, and the subject's control of his/her own information. **However, when the possibility of finding medically significant IFs in a research study is expected to be high, the subjects should be asked during the consent process if they will agree to disclosure by the investigator to their primary care physician.** If the subject does not have a physician, the subject may be offered SBU University Hospital's HealthConnect service, phone # 444-4000, which can provide guidance and appointments with a primary care physician. Stony Brook University Hospital also has a financial assistance/ charity care program which can be reached at 444-4331
    - Depending on the specific IF revealed, the investigator may suggest a specialist, such as an oncologist. To ease the subject's anxiety, the more significant the IF, the more rapidly this step should occur, and the more sensitive the investigator must be in communicating the IF to the subject, using assistance as needed (e.g. notice of possible cancer may require the presence of an oncologist who can immediately address questions and concerns etc.).
    - When future analyses are done on study data that has been de-identified, it may be impossible to let subjects know individual results. However, data should not be de-identified for the sole purpose of avoiding a responsibility to report IFs.

- **The plan for informing subjects in the consent process of the potential for IF's**, including:

    - Probabilities of occurrence (based on available literature),
    - The foreseeable risks and benefits associated with the types of IF's that are possible
    - How the IF's may be uncovered, e.g., during screening, procedures performed for research, future analysis of results, etc.
    - Statement that payment for any clinical follow-up as a result of being informed of an IF will be the subject's responsibility. If the subject, or subject population, has no health insurance, the investigator should advise the subject of available avenues for accessing follow-up or should know to whom to refer the subject for information and counseling. Stony Brook University Hospital also has a financial assistance/ charity care program which can be reached at 444-4331.
    - Statement that any findings, incidental or not, discovered during the course of the research activity, that indicate that the subject may hurt him/herself or others, or that the safety of a child is at risk, is mandated to be reported to applicable authorities.

17.9.5 Incidental Findings (IF) Consent Form Language

NOTE: Adapt to your specific study, based on the assessment/disclosure plan proposed to the IRB, as above. See below for other suggested insertions, as applicable*):

Incidental Findings

The procedures in this study are being done, and results reviewed, only for research reasons, as explained in the beginning of this consent form. In other words, this study is neither designed nor intended to detect health problems.

*Nonetheless, it is possible that during review of results from **(list the procedure/s)**, we may uncover something that may (potentially) have health or reproductive importance to you. Such findings are called 'incidental findings'. In studies like this, the types of incidental findings include **(provide general detail).** The possibility of uncovering these types of incidental findings is **(common/rare).** If this happens, the principal investigator will contact you to discuss what the finding possibly means, if you agree to be told this information. You will then be referred to your medical doctor for follow-up. We can help you secure a medical doctor if you don't currently have one.*

The discovery of an incidental finding may cause you to feel anxious. If you have further tests done by your medical doctor, those results will then become part of your medical record, which may

affect current and future health or life insurance. The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility (financial assistance programs are available, should you need such help).

Do you agree to be informed of any incidental findings discovered during the course of this research study? Choose, and sign below one option:

YES, I want to be informed of incidental findings discovered during the course of this research study

_____ _____

NO, I do not want to be informed of incidental findings discovered during the course of this research study

_____ _____

****Add/amend the above language as applicable. Here are some examples:***

*"The **(scans/tests etc)** that **are/is** done in this study are/is not of the same quality as those done by a doctor for medical reasons."*

And/or

"The investigators of this study are not medical doctors and are not trained to assess these possible findings. Your consent to be in this study also includes permitting the principal investigator to share your data in a confidential manner with experts outside of the study team so that more information regarding the importance of any uncovered incidental findings can be determined."

And/or

"Because of the possible significance of the IF's that may result from these procedures, your consent to be in this study also includes permitting the investigators to disclose IF's not only to you, but directly to your primary care physician, as necessary. If you do not have one, assistance will be provided in securing one"

And/or:

(specifically for MRI studies): "*Most incidental findings represent common minor abnormalities that pose no clinical risk and require no medical referral: for example, one study found that 61 out of 151 participants (40%) had such incidental findings that required no referral. Incidental findings that require medical referral are much rarer: for example, a study of children and young adults found that only 1 out of 225 participants required urgent medical referral, and another study found that only 2 out of 2000 people needed a medical referral for an aneurysm and 1 out of 2000 people needed medical referral for a potentially malignant brain tumor."*

17.9.6 Procedures for IF's that are Not Anticipated

Where an IF occurs that is not anticipated, the event is deemed an unanticipated problem involving risk to subjects, and should be reported immediately to the IRB using the Unanticipated Problems Reporting Form (in electronic management system) for assessment and determination of course of action.

When the potential need to share study findings with a subject has arisen unexpectedly, the PI should submit to the IRB, the plan for communicating the results to the subject. Depending on the study, the plan may need to include transmitting (and confirming transmission of) the information to the subject's primary care physician as well, following subject consent for release of medical information.

See the above section for variables to consider.

17.9.7 Special IF considerations for Children as Research Subjects:

Parents of minor subjects, and minor subjects for whom the IRB has required that assent (either verbal or documented) be obtained, must be informed of the possibility of IFs, as mentioned above. In instances where the child is in the research (or samples may be retained) and passes the age of majority, the consent process s/he undergoes as an adult should include a discussion of IF's. Note:

- When an IF reveals a potentially grave or life-threatening condition, including substance abuse, that requires clinical evaluation (or intervention, in the case of substance abuse), the parent or guardian has a responsibility to learn of this information and act in a way to preserve the child or adolescent's health. The parent permission and minor assent documents should clearly address the possibility of this disclosure.
- In accordance with state law, if the IF is a pregnancy in the minor subject (e.g. detected through screening procedures), the minor subject is to be told. Informing the parent can only be done with the minor's permission to do so. When research studies involving minors test for pregnancy:

- Assent form should read, “If, as a result of the study tests, we find out that you are pregnant, we will tell you so. We will also strongly urge that you discuss these results with your parent or legal guardian so that appropriate health care can be obtained as soon as possible”
    - Parent permission should read, “If, as a result of the study tests, we find out that your child is pregnant, we will tell her so. We will also strongly urge your child to discuss these results with you so that appropriate health care can be obtained as soon as possible.

- In some cases, an IF may reveal sensitive information, e.g. the child is experiencing physical abuse by the parent. In these instances, contact the IRB through the ORC. A plan of action will be developed, in consultation with legal counsel.

17.10 Community Based Participatory Research (CBPR)

CBPR is a subset of community-based research that has the most significant community involvement, from generating research ideas, to conducting the research, to disseminating results back to the community. It is anticipated that CBPR will become an active aspect of the HRPP upon the Institution’s successful application for a Clinical and Translational Science Award (CTSA).

17.11 Proper Documentation in Human Subjects Research

1. Applicability: This guidance applies to all University research involving human subjects (i.e. that qualified for exempt, expedited, or full review), with the exception of pharmaceutical funded/initiated studies. Such studies through the pharmaceutical industry have very specific documentation requirements promulgated by the sponsor and the FDA which must be followed to the letter to ensure the compliant conduct of the clinical trial.
2. Introduction: Detailed documentation is critical for ensuring, and proving, your compliance with federal regulations and University policies for the conduct of any and all research involving human subjects. This guidance provides details for proper documentation in research involving human subjects. When ORC Staff conduct audit/monitoring visits, it will be expected that appropriate documentation processes are being followed.
3. There should be two types of ‘stories’ that must be clearly documented for each study (A) The Regulatory Binder and (B) The Subject Record.

(A) The Regulatory Binder: The Regulatory History of the Study

Note: Some, but not all, of the documents below may already be available in the IRB electronic system. If the PI decides not to place those documents in the regulatory binder for the study, the PI

is responsible for ensuring that all study personnel know how to access them *in the electronic system.*

The following documents should be in this binder, in sequential order, with most current documents on top:

1. IRB approval, acknowledgement letters.
2. All IRB approved/acknowledged study documents (e.g. protocol, protocol amendments, stamped consent/permission/assent documents, diary forms, translations, advertisements/brochures for recruitment, surveys), package inserts, Investigator brochures, Certificate of Confidentiality, etc.).
3. Protocol deviations/exceptions with report to the IRB (and sponsor as applicable), and resulting determinations and IRB approved corrective action plans, if required.
4. Unanticipated problems involving risk to subjects or others (UP's): with report to IRB, and their determination.
5. Data collection form (sometimes called Case Report Form) templates. A case report form is a data collection tool used to help investigators capture all research-required information for each subject. It is an excellent tool to ensure that the protocol is followed as approved by the IRB. For investigator initiated studies, a case report form/source document collection form can be created by going through the protocol and outlining, step by step, what research procedures will occur, and what data was collected at each study visit. The web has many sites to aid in the construction of case report forms or data collection forms. (for example see: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4170533/ or http://www.bumc.bu.edu/irb/files/PDFs/ABB_CaseReportForms_ClinicalResear...)
6. Inclusion/Exclusion Checklist template, with acceptable ranges (i.e. lab values, ages, etc.), and a line for the subject's value, where applicable. PI should review and sign the completed checklist for each subject, prior to any research procedures being conducted on the subject (including screening, randomization etc.). Although this requirement is currently in place only for more than minimal risk studies, it is strongly suggested that all studies adopt the practice to ensure that only IRB approved, eligible subjects are enrolled in the study.
7. Delegation of Authority Form: With this document, the PI formally delegates authority to specific team members to do specific research-related tasks. The delegation must be consistent with the individuals' expertise and licensure where applicable (e.g. Ms. S. Coordinator: consent process; Dr. C. Investigator, conducts the neuropsychological exams; Mr. G. Student: data input/analysis etc.). This document should also show team members signatures and initials (for audit purposes).
8. Proof of licensure for team members, based on their delegation of authority from the PI, as above.
9. Subject ID code list location

10. Subject screen log/Subject enrollment log: this allows you to document the chronological enrollment of subjects
11. Monitoring visit reports from within or outside the University, self-audit reports
12. Relevant communications: e-mails, telephone call notes relating to the conduct of the study, or subject queries or complaints etc.

And, as applicable:

1. Drug/device dispensing log
2. Reports required by sponsors, if any, and resulting correspondence
3. Decoding procedures (for blinded trials)
4. Certificate of Confidentiality
5. FDA Forms (e.g., 1571), reports to FDA, FDA communications, DSMB reports (if the PI is the sponsor of an IND/IDE)
6. Location of stored/archived research records
7. Membership of the Data Safety Monitoring Board

(B) The Subject Record: The Complete "Story" for Every Subject

There should be a record of all activities that have occurred on the study for each subject.

The record should be coded, and the key to the code should be retained in a separate locked location in order to protect subject confidentiality.

1. **Description of method of recruitment** for the subject in question (e.g. "Ms. Patient was encountered in the clinic when she came for a medication check for her thyroid", or Mr. Grad Student responded to an advertisement in Psych B. etc.)
2. **Completed inclusion/exclusion checklist** with specific values/data entered for the subject. *Although this requirement is currently in place only for more than minimal risk studies, it is strongly suggested that all studies adopt the practice to ensure that only IRB approved, eligible subjects are enrolled in the study.*
3. **Details of the consent process** with the subject. A form can be used to facilitate this documentation, an example of such, is provided in Appendix I following this SOP.
4. **Signed informed consent/permission/assent documents** (including any consent addenda signed by the subject during the course of the study).
5. **Source documents:** A source document contains data that is initially collected on the subject. It can be a case report form/data collection form or may simply be lab values, etc.

The source documentation details the specific values/data entered for the subject, i.e., inclusion/exclusion data, screening, research procedures conducted/data collected throughout the course of the study. Such information must match what the informed consent documents

describe will be conducted/collected. Examples: hard copies of completed surveys, questionnaires, lab/radiology reports, x-rays.

Note: If information is taken from the medical record, a copy of the applicable page (or screen shot from the electronic medical record) will suffice as source documentation.

6. **Completed case report forms/data collection forms for each visit.** These should also provide a section where the investigator can put 'visit notes' (e.g. subject reported no problems etc.)
7. **A log of all adverse events (AE's) that the subject experienced** (if it does not constitute an unanticipated problem involving risks to subjects or others, which must be reported to the IRB immediately. These AE's are reported at the time of continuing review.

Appendix I Documentation of Consent/Permission/Assent Process

(To be completed by the Study Team Member who is Obtaining Consent)

Study PI:_____

Study Identifier:_____ **Date:** _____

Subject Name: _____

Parent Name(s), if subject is a minor_____

Circle answer:

1. Have you been delegated authority by the Principal Investigator to conduct consent processes for this study? Y N N/A (You are the PI)

2. Did you first verify that the consent document being used is the most current IRB approved/stamped version, obtained either from the electronic system, or the study regulatory binder? Y N

3. Did you discuss with the subject/parent:
    1. The purpose of the study Y N
    2. Possible risks and benefits Y N
    3. All research procedures Y N
    4. Alternatives to being in study Y N
    5. Participation is voluntary Y N
    6. Subject can withdraw at any time Y N

4. Did the subject/parent exhibit an appreciation of:
    1. The purpose of the study Y N
    2. Possible risks and benefits Y N
    3. All research procedures Y N
    4. Alternatives to being in study Y N
    5. Participation is voluntary Y N
    6. Subject can withdraw at any time Y N

5. Was the subject/parent given an opportunity throughout the process to ask questions? Y N
6. After consent process, was the subject/parent given time to review the consent form? Y N
7. Was the subject given a copy of the IRB approved/stamped, signed consent form? Y N

Your signature below confirms the accuracy of the information provided above, and certifies that no study procedures were performed prior to the subject signing the consent document.

_____ _____

Printed Name Signature Date

17.12 Genomic Data Sharing (GDS) for NIH Grant Submissions

NIH GDS (Genomic Data Sharing) Policy applies to:
1. <u>All</u> NIH-funded research that generates large scale (> than 100 individuals) human or non-human genomic data (e.g., SNP arrays, genome sequencing, RNA sequencing, transcriptomic, metagenomic, epigenomic and gene expression data), as well as the use of these data for subsequent research sharing in NIH-supported repositories; and
2. All research involving genotype/phenotype data that will be submitted to one of the NIH-supported repositories, <u>even if the research itself is not NIH-supported</u>:

- Database of Genotypes and Phenotypes (dbGaP),
- Gene Expression Omnibus (GEO),
- Sequence Read Archive (SRA), or the
- Cancer Genomics Hub.

When does the Policy NOT apply?

- When the genomic data is generated without NIH funds (unless the researcher voluntarily requests submission to one of NIH-supported repositories)

- When NIH-funded research for projects involve instrument calibration exercises, statistical or technical methods development, or the use of genomic data for control purposes, such as for assay development
- When the following funding is requested: Institutional Training Grants (T32s, T34s, T35s, and TL2s), K12 Career Awards (KL2s), Individual Fellowships (Fs), Resource Grants and Contracts (Ss), Linked awards derived from previously reviewed applications, or facilities or coordinating centers funded through related initiatives to provide genotyping, sequencing, or other core services in support of GDS.

When NIH funding is requested for a grant proposal, the researcher should do the following:

- Provide a basic plan for following the GDS policy, located in the Resource Sharing Plan section of funding applications. (The Genomic Data Sharing Plan template available in the electronic management system should be reviewed. Complete and upload with the applicable IRB submission.)
- If broad sharing of genomic data is not possible, include an explanation.

Just-In-Time awards:

NIH will require the following documentation at Just-In-Time:

- An IRB approval letter for your human subjects protocol, and
- An Institutional Certification (available through the Office of Research Compliance) to be completed and signed by the researcher, and then submitted to the Office of Research Compliance for an authorizing signature

Required when genomic data needs to be submitted to an NIH-supported data repository, but NIH is not the funder and/or a funding request is not involved:

The IRB will be responsible for the authorizing signature on the Institutional Certification.

Consent document language for subjects when genetic data will be deposited in NIH-supported repositories:

The consent templates in the Forms Library of the electronic management system contain instructions on language to be used when genetic data is to be deposited in NIH-supported repositories.

Resources

The Genomic Data Sharing Policy

Implementation of the NIH Genomic Data Sharing Policy for NIH Grant Applications and Awards

Research Involving or Generating Genetic Information

Research that generates or uses genetic information may create special risks to human subjects and their relatives. These involve medical, psychosocial, legal and economic risks, such as the possible loss of privacy, insurability, and employability, and may result in stigmatization and discrimination. Information about one's own genetic make-up may also provide information about family members.

In studies involving genetic testing or analysis of genetic information, several questions should to be addressed to ensure that potential risks are well understood and that the rights and interests of subjects and their family members are carefully considered and planned for. For example:

1. Is the testing intrinsic to the study? If not, has participation in the genetic testing component been provided as an opt-in?
2. Will test results be given? Is there an appropriate plan for return of results?
3. Does the subject or family member be provided the option to receive or not receive results? How will this decision be recorded?
4. Could the results provide information about individual disease risk? Disease risk for family members?
5. Could other clinically relevant information or incidental findings be uncovered by the study? Is there a plan for the management of such findings?
6. Will testing that could produce clinically relevant information occur in a CLIA-certified lab? If not, are there tests available that could validate or support findings?
7. Could a change in a family relationship be disclosed, such as mistaken paternity?
8. Could/will the research provide information about the origins, ancestry, or natural history of families, indigenous peoples, tribal populations, or other populations? What are the possible risks?
9. Could/will the research generate information that could place subjects or family members at risk or be stigmatizing?
10. Could/will the research generate information of other value or importance to subjects/families?
11. Do any practical limitations exist on the subject's right to withdraw from the research, withdraw data, and/or withdraw biological materials (e.g., specimens, cell lines, extracted genomic DNA)?
12. How will the information and/or biological materials be protected and who will have access?

13. What is the potential for re-identification of individual subjects (e.g., through the combination of their genetic information and/or materials with other sources of information (e.g., public records))? What measures can be taken to mitigate these risks?
14. Is a Certificate of Confidentiality (CoC) in place or should one be considered? (See Section 17.17)
15. Will the specimens, cell lines, or genetic information be stored and/or made available for future research? Is this provided as an opt-in when not intrinsic to the study? (See Section 7.6)

Investigators should carefully consider the above and other factors relevant to their specific study when developing the protocol, consent process, and consent form. The President's Bioethics Commission, the National Academies of Sciences, Engineering, and Medicine, and others have produced reports, recommendations, and materials that investigators and the IRB may find helpful in protocol development and review, including:

- Returning Individual Research Results to Participants: Guidance for a New Research Paradigm
- Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts
- Privacy and Progress in Whole Genome Sequencing
- Genetics Research and American Indian and Alaska Native Communities
- National Human Genome Research Institute:
  - Human Subjects Research in Genomics
  - Return of Research Results
  - Data Sharing and Privacy
  - Informed Consent for Genomics Research

In addition to the ethical considerations, investigators must ensure that research involving genetic testing or use of genetic information is consistent with applicable law (e.g., GINA, HIPAA, EU GDPR, state law) and policy (e.g., NIH).

General Data Protection Regulation (GDPR)

GDPR is a regulation based on the protection of data and privacy of individuals in the 28 EU member states and three additional countries (Liechtenstein, Iceland, and Norway), which together constitute the greater European Economic Area (EEA).

GDPR applies to:

- Organizations anywhere in the world that process the personal data of those in the EEA related to offering of goods and services, regardless of whether payment is exchanged.
- Organizations anywhere in the world that monitor the behavior of subjects as far as their behavior takes place in the EEA.

- GDPR likely applies to a study if the researcher continues to monitor the EEA research subjects or provides study related interventions after they return to the EEA (In this case, the Sponsor is not located in the EEA).

GDPR does not apply to:

- Organizations not present in the EEA which process the personal data of citizens of EEA member countries while they are abroad in non-EEA countries (e.g., if an EU citizen travels to the US, a company in the US processing personal data the EU citizen leaves behind while visiting the US is not subject to GDPR. However, if that same company processed data the same EU citizen generated while in the EEA, that activity would be subject to GDPR.

Certain types of personal data require care in handling, and this data is often the type collected in research studies. Personal Data broadly means any information relating to an identified or identifiable natural person. An identifiable natural person is "one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that person." The GDPR frequently requires that data revealing any of the following considered to be "sensitive" data be collected through an informed consent process:

- Racial or ethnic origin
- Political opinions
- Religious or philosophical beliefs
- Trade union membership
- Genetic, biometric, and health data
- Data concerning a person's sex life or sexual orientation

Specific language must be inserted into the informed consent form if GDPR applies. Contact the Office of Research Compliance if your study will be enrolling GDPR subjects. The GDPR Consent language may be added to a Common Rule Consent Form. In that way, the EEA Research Subject will need to sign the document to provide both the informed consent required by U.S. federal law and the GDPR Consent.

General Data Protection Regulations do not apply when the collection of data does not include information that is linked to a subject's identity such as an anonymous survey in which the identity of the subject cannot be traced to the individual.

Another key point of GDPR is whether the data is anonymized (i.e., impossible to connect back to a single person). Fully anonymized data is not subject to GDPR. Coded research data is considered to be "Pseudonymized Data" and therefore Personal Data under the GDPR because the data can be

attributed to a person by the use of additional information such as a key to the code. If the researcher maintains the key (or a third party maintains the key for the researcher), such data will generally not be treated as anonymized Personal Data under the GDPR. Full anonymization of Personal Data requires not only the removal of all identifiers from the data set, but also the destruction of any keys to the code. Pseudoanonymized data is data that may be able to be connected back to identifiable information. Additionally, the GDPR applies when the university conducts research in the US in which subject data is transmitted to a sponsor, server, or data core facilities in the EU.

Genetic Information Nondiscrimination Act (GINA)

GINA generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against individuals based on their genetic information. This law protects individuals, including research subjects, in the following ways:

- Health insurance companies and health plans are generally prohibited from requesting or requiring genetic information of an individual or their family members, including genetic information generated from research;
- If health insurance companies and health plans do receive such genetic information, they may not use it to make decisions regarding coverage, rates, or preexisting conditions; and
- Employers with 15 or more employees generally may not use genetic information for hiring, firing, promotion, or other decisions regarding terms of employment.

GINA's protections do not extend to life insurance, disability insurance, or long-term care insurance.

GINA defines genetic information as information about:

- An individual's genetic tests;
- Genetic tests of an individual's family members;
- Genetic tests of any fetus of an individual or family member who is a pregnant woman, and genetic tests of any embryo legally held by an individual or family member utilizing assisted reproductive technology;
- The manifestation of a disease or disorder in an individual's family members (family history); or
- Any request for, or receipt of, genetic services or participation in clinical research that includes genetic services (genetic testing, counseling, or education) by an individual or an individual's family members.

GINA includes a "research exception" that allows health insurers and health plans who are engaged in research to request, but not require, that an individual undergo a genetic test so long as certain requirements are satisfied. Additional information on GINA and this exception are

available on this OHRP website.
The Stony Brook University IRB will consider the protections and limitations of GINA when it assesses the risks of research generating or using genetic information and the adequacy of the measures to protect privacy and maintain confidentiality. Generally, the IRB will also require that the protections and limitations of GINA are disclosed in the consent process when applicable.

Genomic Data Sharing (GDS)

(The information in this section is largely derived from NIH policy and materials. While the processes (e.g., for IRB submissions/review) should be modified to reflect organizational practice, other substantive changes should be verified against the information on NIH's websites. NIH has purposely set a higher standard than is required by regulation: "…the NIH GDS Policy requires that informed consent be obtained for the future research use and broad data sharing of de-identified data from biospecimens created or collected after January 25, 2015 (the effective date of the GDS Policy). While the Common Rule does not require informed consent for research with de-identified biospecimens or cell lines, the GDS Policy establishes expectations and protections beyond those of both the current, and the revised Common Rule … because the evolution of genomic technology and analytical methods may raise the risk of potential re-identification.")

Stony Brook University complies with the NIH GDS Policy, which allows for "broad and responsible sharing of genomic research data", via submission of said data into an NIH-designated data repository. The intent of NIH's policy is to speed discoveries to diagnose, treat, and prevent disease. **To ensure consistency in the protection of human subjects, Stony Brook University applies the NIH principles for informed consent and for a genomic data sharing plan to all research that involves or contemplates genomic data sharing.**

The NIH policy applies to grant activities requesting support from NIH for research involving the generation of large-scale human (and/or non-human) genomic data, regardless of funding level, such as:

- Research project grants (Rs);
- Program projects (Ps) and SCORs (Ss);
- Cooperative agreements for research (Us);
- Individual career development awards (Ks) that include a research component;
- "S" activities that include a research component; and
- All other activities that include a research component.

Also covered under this policy is research involving data derived from these activities for subsequent research. All basic and clinical research, including clinical trials, supported by NIH that involves the generation or use of large-scale genomic data fall within the scope of the policy.

The policy does not apply to:

- Institutional training grants (T32s, T34s, T35s, and TL2s);
- K12 career development awards (KL2s);
- Individual fellowships (Fs);
- Resource grants and contracts (Ss);
- Linked awards derived from previously reviewed applications (KL1, KL2, RL1, RL2, RL5, RL9, TL1, UL1);
- Facilities or coordinating centers funded through related initiatives to provide genotyping, sequencing, or other core services in support of GDS.

Because of the potential for re-identification of genomic data, Certificates of Confidentiality (CoCs) are automatically issued by the NIH for any research it supports, in part or in whole, that involves *"the generation of individual level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is recorded in such a manner that human subjects can be identified or the identity of the human subjects can readily be ascertained as defined in the Federal Policy for the Protection of Human Subjects (45 CFR 46)."* Research covered by the NIH policy and/or the underlying PHS Act is protected by the CoC in perpetuity; as such any downstream recipients of such information must comply with the requirements of the PHS Act.

Investigators without NIH support who intend to submit genomic data to a NIH repository are encouraged to obtain a CoC. Investigators conducting research generating or using genomic data are encouraged to obtain a CoC when one is not already in place (e.g., for downstream use of data that was collected under a CoC.

Definitions

Genomic data: information derived from study of an organism's genome, i.e., the set of DNA (including all the genes within) in every cell that provides all of the information needed to build and maintain that organism.

Large-scale data include genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, epigenomic, and gene expression data. Examples of genomic research projects that are subject to the Policy and the timeline for submission and sharing of data from such projects may be found here: https://osp.od.nih.gov/wp-content/uploads/Supplemental_Info_GDS_Policy.pdf

NIH-Designated Data Repository: any data repository maintained or supported by NIH either directly or through collaboration. Examples of such repositories is available here:

https://osp.od.nih.gov/scientific-sharing/data-repositories-and-trusted-partners/. Data may be unrestricted or controlled access:

- **Unrestricted-Access ("Open Access"):** data are publicly available to anyone (e.g., The 1000 Genomes Project)
- **Controlled-Access:** the data are available to an investigator for a specific project only after the investigators and institution certify to abide by specified terms and conditions and NIH has approved the use (e.g., dbGaP)

Procedures

IRB Submissions and GDS

For any cell lines created or specimens to be collected, analyzed, and shared subject to the GDS Policy, the IRB expects that informed consent will be obtained from the research subject for the future research uses and broad sharing of data required under the policy. **This is the case even if the specimens or cell lines are de-identified.** If there are compelling scientific or legal reasons that necessitate the use of genomic data from cell lines or clinical specimens that lack consent for research use and data sharing, investigators will need to provide a justification in the funding request to NIH for their use. The funding NIH institute/center will review the justification and decide whether to make an exception to the consent expectation. Exceptions from the NIH are not required if only some participants decline to consent to broad sharing, rather an exception request must be granted by NIH for research when consent for broad sharing has not or will not be sought.

Subjects asked to allow for future research uses and broad sharing of their genomic data have the ability to decline, and still remain in the research (however their data cannot be placed into a repository or otherwise broadly shared). The only exception to this is when sharing of the data is intrinsic to the study (e.g., the purpose of the study is to establish a repository for sharing biological specimens and/or data for future research).

Sample consent language for studies subject to GDS is available in the consent template, from the HRPP/IRB Office.

Applications to the Stony Brook University IRB should include information about the proposed generation or use of genomic data including, as applicable:

- Whether the research will generate or use data subject to the NIH GDS policy;
- The name of the NIH data repository/database, or other repository or database, that data will be submitted to or acquired from;

- Whether the data is restricted access or unrestricted access;
- Whether there are any data use limitations or modifiers (e.g., use limited to a specific disease, restricted to not-for-profit organizations, IRB approval requirement, etc.);
- The plan for informed consent and the proposed consent language;
- Details regarding the storage of data or specimens for future use; and
- A copy of the genomic data sharing plan.

The IRB will review the proposal for genomic data sharing or subsequent use of such genomic data in accordance with the criteria for approval of research and the guidelines for IRBs provided by NIH.

When Stony Brook University is responsible for NIH Institutional Certification (see below), the IRB review will specifically address the required assurances outlined on the Extramural Institutional Certification. When appropriate, if the IRB is unable to confirm that a certification element is satisfied (e.g., because the IRB has not yet granted final approval), Provisional Institutional Certification will be provided.

Grant Applications and GDS

Investigators planning to apply to NIH for research that will generate large-scale human genomic data as defined above should contact the appropriate NIH Program/Project officials to discuss expectations and timelines for complying with this policy. Along with the grant, the following will need to be submitted:

- **Notification in a cover letter** of the intent to generate large-scale human genomic data
- **A genomic data sharing plan,** within the grant's resource sharing plan section (NIH guidance on these plans is available here: https://osp.od.nih.gov/wp-content/uploads/NIH_Guidance_Developing-GDS_Plans.pdf)
- **Institutional Certification** from the Office of Sponsored Programs (templates available here: https://osp.od.nih.gov/scientific-sharing/institutional-certifications/). Certification must be provided for all sites contributing samples. If more than one site is contributing samples, the primary site may submit one certification on behalf of all collaborating sites (or each site may provide their own certification if this is the site's preference). This certification assures that:
    - The data submission is consistent with applicable national, tribal, and state laws and regulations, and institutional policies;
    - Any limitations on the research use of the data, as expressed in the informed consent documents, are delineated within the certification;
    - The identities of research participants will not be disclosed to the repositories;
    - An IRB and/or Privacy Board has reviewed the investigator's proposal for data submission and assures that:

- the protocol for the collection of genomic and phenotypic data is consistent with human subjects regulations;
- data submission and subsequent data sharing for research purposes are consistent with the informed consent of study participants from whom the data were obtained;
- consideration was given to the risks to participants and their families, and, to the extent relevant and possible, to groups or populations associated with the submission and subsequent sharing of the data; and
- that the investigator's plan for de-identifying datasets is consistent with the standards outlined in the NIH Genomic Data Sharing (GDS) Policy.

- **In situations where the sharing of human data is not possible** (i.e., the Institutional Certification criteria cannot be met), a justification is required to explain why these data cannot be shared, and an alternative data sharing plan will need to be provided. Exceptions to NIH expectations for data submission to an NIH-designated data repository will be considered on a case-by-case basis by the NIH funding Institute or Center (IC).

Investigators who wish to use controlled-access human genomic data from NIH-designated data repositories (e.g., dbGaP) should briefly address their plans for requesting access to the data and state their intention to abide by the NIH Genomic Data User Code of Conduct in the Research Plan of the application. The code of conduct is available here: https://osp.od.nih.gov/wp-content/uploads/Genomic_Data_User_Code_of_Conduct.pdf . Access to controlled-access data is dependent on an approval process that involves the relevant NIH Data Access Committee(s). Applicants may wish to secure access to the data prior to submitting their application for NIH support. Secondary users of controlled-access data are not expected to deposit their findings into NIH-designated data repositories, unless appropriate.

Investigators who wish to use/download data NIH unrestricted-access repositories should not attempt to identify individual human research participants from whom the data were obtained, and, in all oral and written presentations, disclosures, or publications, acknowledge the specific dataset or accession numbers and the repository through which the data were accessed.

Procedures for submitting data into, or requesting access for data from an NIH-designated repository, are available here: https://osp.od.nih.gov/scientific-sharing/researchers-institutional-certifications/.

17.13 ResearchMatch as a Recruitment Tool

The University is a part of ResearchMatch (RM), the national registry that connects researchers with volunteers who wish to get involved in research studies. This national registry provides a

secure, web-based approach to address a key barrier to advancing research: participant recruitment.

This new tool allows investigators to conduct targeted searches for potential volunteers based on location and specific demographics.

Investigators may register for feasibility access to assess the functionality of the registry and explore the database to determine how many people registered in ResearchMatch might fit the criteria for a future study or one that is currently ongoing:

1. Go to https://www.researchmatch.org/
2. Click "Researchers" at the top of the page
3. Green button "Register Now" (If you think you'll need help registering, click on the tutorial link below the green button)
4. Select "Stony Brook University" as the institution
5. Type in your Stony Brook email address
6. Retrieve verification code from your email, cut and paste it into RM
7. Read site instructions
8. Read Researcher Acknowledgement form and "ACCEPT"

To use this recruitment tool, researchers are required to submit individual requests for approval by the IRB. The "ResearchMatch Recruitment Method Instructions", available in the electronic management system library, provides the details for adding this recruitment method to both new and existing studies. Once you have IRB approval for your study, including an approved RM contact message, one of the RM liaisons can approve your message to be sent to registered RM users (i.e., potential subjects). If a user is interested in volunteering for your study, they accept your invitation and release their information to you for direct contact.

17.14 Conducting Research in a Clinical Setting (e.g., University Hospital): Special Considerations

Hospitals are unique settings in which to conduct research, as the responsibilities and priorities of research teams and clinicians must be carefully balanced when it comes to interacting with patients who may be, or may be approached to become, subjects.
Key points to keep in mind are:

- Clinical management always takes precedence over the requirements of a research protocol. That being said, if a protocol deviation occurs (whether due to competing clinical management or for any other reason), it should be reported to the IRB, as soon as possible.
- Communication between researchers and clinicians is important:

- Researchers should consult with the patient's nurse or other health care provider before approaching the patient for recruitment, consent process, or for the conduct of research procedures.
- A copy of the research consent must be in the EMR.
- A copy of the current protocol must be on the unit or be readily available for clinical staff to review if necessary. Cerner Powertrials should be in use by Study Coordinators to post the protocol and I/E criteria for their respective studies as well as note when a patient is a participant on a study.

- If issues or questions arise and cannot be readily resolved, contact should be made with the unit supervisor, Assistant Director of Nursing, PI and/or treating MD.
- All research visits must be thoroughly documented in EMR, so all parties are aware of all procedures, clinical or research that have been conducted on the patient/subject.

17.15 Additional Requirements for Studies Funded by the Department of Defense

The Department of Defense defines the term “experimental subject” as an activity for research purposes, where there is an intervention or interaction with a human being for the primary purpose of obtaining data regarding the effect of the intervention or interaction.
10 U.S.C.980 prohibits, subject to very limited exceptions, the use of DoD funds for research involving a human being as an experimental subjects except with the informed consent of the subject or the legal representative. If the research participant does not meet the definition of “experimental subject,” the IRB is allowed to waive the consent process.
32 CFR Part 219 is DoD’s adoption of the “Common Rule” for the protection of human research subjects. This part requires Institutional Review Board approval of human subject research and informed consent for such research subject to waiver in certain cases involving minimal risk. A waiver of informed consent must be obtained from the Assistant Secretary of Defense for Research and Engineering and only if the following criteria are met:

- The research is necessary to advance the development of a medical product for the ilitary Services.s
- The research directly benefits the individual experimental subject.
- The research is conducted in compliance with all other applicable laws and regulations.
- Classified research, does not allow for a waivers of consent.

1. IRB staff, Chair, and members; and researchers and research staff become aware of the specific requirements contained in DoD requirements and educated about these requirements when appropriate once they are notified that the DoD is funding the study.
2. Additional safeguards for research conducted with international populations may be required by the IRB. These can include verification from the country that the research can be carried out. Review by a local context reviewer is necessary to ensure that cultural

norms are integrated into the research and that the researcher has permission to conduct research in that country. Researchers must follow all local laws, regulations, customs, and practices.

3. Records must be maintained that document compliance or non-compliance with DoD requirements and will be made accessible for inspection and copying by representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD Component.
4. The consent form must contain language that allows for the independent inspection of the research which can include the subject's identifiable information or Protected Health Information.
5. When appropriate, research protocols must be reviewed and approved by the IRB prior to the Department of Defense approval. Consult with the Department of Defense funding component to see whether this is a requirement. Protocols must be limited to the DoD funded activities as stated in the approved Statement of Work. Therefore, the HPRO requires the submission of a new, separate protocol that only contains the DoD funded or supported activities. The DoD strongly suggests that the Principal Investigator provide a copy of the protocol to the research subjects with proprietary and personal information redacted as needed.
6. The DoD Component must conduct an appropriate administrative review of the research involving human participants. The DoD Component administrative review must be conducted before the research involving human participants can begin, to ensure compliance with all applicable regulations and policies, including any applicable laws and requirements and cultural sensitivities of the country when the research is conducted in a country other than the United States.
7. Surveys performed on DoD personnel must be submitted, reviewed, and approved by the DoD after the research protocol is reviewed and approved by the IRB. When a survey crosses DoD Components, additional review is required.
8. Employees of the Department of Defense (including temporary, part-time, and intermittent appointments) may not be able to legally accept payments to participate in research and should check with their supervisor before accepting such payments. Employees of the Department of Defense cannot be paid for conducting research while on active duty.
9. Service members must follow their command policies regarding the requirement to obtain command permission to participate in research involving human subjects while on-duty or off-duty.
10. Components of the Department of Defense might have stricter requirements for research- related injury than the DHHS regulations.
11. There may be specific educational requirements or certification required.
12. When assessing whether to support or collaborate with this institution for research

involving human subjects, the Department of Defense may evaluate this institution's education and training policies to ensure the personnel are qualified to perform the research based on the complexity and risk of the research.

13. DoD institutions collaborating with non-DoD institutions may rely on a collaborating non-DoD institution's IRB if the following conditions are met:

- Each institution engaged in non-exempt human participant research must have a current federal assurance of compliance.
- The involvement of DoD personnel in the conduct of the research is secondary to that of the non-DoD institution.
- The DoD institution, non-DoD institution, and the non-DoD institution's IRB have a written agreement defining the responsibilities and authorities of each organization in complying with all legal requirements. This agreement must be approved by the DoD Component prior to the DoD institution's engagement in the research.

14. Determinations of serious or continuing non-compliance, unanticipated problems involving risks to participants or others, or suspension or termination of DoD-supported research must be promptly (no longer than within 30 days) reported to the DoD human research protection officer.

15. The following must be promptly (no longer than within 30 days) reported to the DoD human research protection officer:

- When significant changes to the research protocol are approved by the IRB.
- The results of the IRB continuing review.
- Change of reviewing IRB.
- When the organization is notified by any federal department, agency, or national organization that any part of the HRPP is under investigation for cause involving a DoD-supported research protocol.

16. When research involves U.S. military personnel, policies and procedures require limitations on dual compensation:

- Prohibit an individual from receiving pay or compensation for research during duty hours.
- An individual may be compensated for research if the participant is involved in the research when not on duty.
- Federal employees while on duty and non-Federal persons may be compensated for blood draws for research up to $50 for each blood draw.
- Non-Federal persons may be compensated for research participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.

17. When conducting multi-site research, a formal agreement between organizations is required to specify the roles and responsibilities of each party.
18. Other specific requirements of the Department of Defense research be found in the

"Additional Requirements for Department of Defense (DoD) Research" section in the IRB's "WORKSHEET: Additional Federal Criteria."

19. The IRB considers the appointment of a research monitor:
- Required for research involving greater than minimal risk, although the IRB or organizational official can require this for a portion of the research or studies involving no more than minimal risk, if appropriate.
- The research monitor is appointed by name and shall be independent of the team conducting the research.
- There may be more than one research monitor (e.g., if different skills or experience are needed.)
- The monitor may be an ombudsman or a member of the data safety monitoring board. The IRB must approve a written summary of the monitors' duties, authorities, and responsibilities.
- The IRB or HRPP official shall communicate with research monitors to confirm their duties, authorities, and responsibilities.

20. When research involves U.S. military personnel, superiors of service members (e.g., unit officers, senior NCOs, and equivalent civilians):
- Are not permitted to influence the decision of their subordinates.
- May not be present at the time of recruitment.
- Have a separate opportunity to participate.
- When recruitment involves a percentage of a unit, an independent ombudsman must be present. Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements.

21. Research involving prisoners cannot be reviewed by the expedited procedure.

Additional Requirements for Department of Justice Funded Research
- All projects are required to have a privacy certificate approved by the NIJ Human Subjects Protection Officer.
- All researchers and research staff are required to sign employee confidentiality statements, which are maintained by the responsible researcher.

For National Institute of Justice (NIJ) funded research the consent document must disclose the name(s) of the funding agency(ies).

17.16 IRB Reliance/Single IRB (sIRB) Review

All non-exempt human subject research (or exempt research for which limited IRB review takes place pursuant to §_.104(d)(2)(iii), (d)(3)(i)(c)) that SBU is engaged in must be reviewed and approved by the SBU IRB or an external IRB that SBU has agreed to rely upon prior to the initiation of the research. Phase I research must be reviewed by the Stony Brook University IRB

unless circumstances require that the study be reviewed by an external IRB.

SBU investigators involved in multi-site research are encouraged to discuss with collaborators the possibility of shared IRB review, i.e., having one IRB review on behalf of all sites.

If the research is part of a multicenter grant awarded from NIH https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html or a cooperative research project under the revised common rule provision https://grants.nih.gov/grants/disclaimer.htm, a single IRB (sIRB) review is required in most circumstances. The reader is referred to Section 17.16.5 for details specific to compliance with the NIH sIRB policy or revised Common Rule cooperative research provision.

Investigators should contact the Reliance Administrator in the Office of Research Compliance early in the multi-site grant/contract process to discuss possible sIRB options as discussed in section 17.16.2 (SBU Serving as the Reviewing IRB) and section 17.16.3 (SBU Ceding Review to an External IRB) below.

17.16.1 Reliance Agreements

Reliance agreements must be in place for all shared IRB review arrangements. The Reliance Administrator ensures that these agreements are negotiated to reflect study-specific, respective responsibilities of the reviewing IRB and the relying Institutions.

The Reliance Agreement:

- Documents the respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.
- Describes the responsibilities of all parties and how communication between parties will occur, for example, notifications of the outcome of regulatory review and management of federally-mandated reports such as reports of unanticipated problems, serious or continuing noncompliance, and suspensions or terminations of IRB approval.
- When IRB certification requirements apply (e.g., for NIH Genomic Data Sharing, Certificates of Confidentiality), the agreement or written procedures will indicate who is responsible for meeting the certification requirements.
- Specifies contact information and personnel for both the sIRB and relying institution(s).
- Addresses whether the relying organization applies its FWA to some or all research, and ensures that the IRB review is consistent with requirements in the relying organization's

FWA.

- Addresses which organization is responsible for obtaining any additional approvals from DHHS when the research involves Subpart B, C, or D determinations.

The institution that is awarded the funding for the research is responsible for maintaining all agreements and for ensuring that adequate and appropriate communication channels between the sIRB and participating sites are in place. Participating sites are responsible for maintaining copies of the site agreement in accordance with the terms of their FWA.

17.16.2 SBU Serving as the Reviewing IRB

Factors Considered by the ORC to have SBU provide IRB Services

The Reliance Administrator evaluates the following factors, and others as appropriate, when considering a request for an SBU IRB to serve as the IRB of record for a particular study or studies:

1. The terms of the external site(s) FWA;
2. The accreditation status of the external site(s)
3. Prior experience with the site(s) and investigators;
4. The compliance history of the site(s) and investigators (e.g., outcomes of prior audits or inspections, corrective actions);
5. The research activities to be conducted at the external site(s);
6. The willingness of the external site(s) to accept SBU's reliance terms and procedures; and/or
7. The ability of the site(s) to collaboratively provide meaningful oversight of the proposed research, taking into account factors such as:
   a. The risks and procedures of the research;
   b. The resources available at each site and ability to accommodate or collaborate with each other in observing the consent process, performing compliance reviews, investigations of potential noncompliance, and similar matters;
   c. The expertise and experience of the SBU IRB with the proposed research, subject population, and applicable regulations;
   d. The ability of the SBU IRB to comply with the relevant local context considerations of the external site(s), as provided by that site(s); and/or
   e. The willingness or ability of the external site(s) to provide information and respond to questions regarding investigator qualifications, conflicts of interest, organizational requirements, local context, and other matters that may inform the IRB of record.

The Reliance Administrator will present relevant factors for consideration by the IO or AVP-RC,

who will make the final decision regarding whether or not the SBU IRB will serve as the IRB or record. The PI will be notified of the decision.

17.16.3 Responsibilities when SBU is the Reviewing IRB

1. Responsibilities of the SBU IRB

- Policies and procedures in the conduct of review for all sites (SBU and external) will mirror those outlined throughout these SOPs, as set forth in Domain II of the AAHRPP accreditation standards. Possible exceptions are noted in section 17.16.4. Additionally, the following SBU IRB responsibilities are to be applicable for all sites:
  - Have the final authority to decide whether SBU or external researcher or research staffs' COI and its management, if any, allows the research to be approved
  - Have the authority to request an audit of research being reviewed.
  - Make relevant IRB policies readily available to relying external sites, including their HRPP staff, researchers, and research staff, and ensure that changes to those policies are communicated as well.
  - Ensure that an ORC contact person along with contact information is specified for researchers and research staff to obtain answers to questions, express concerns, and convey suggestions regarding the SBU IRB.
- Adding sites to an already approved IRB study will be considered a modification, and will be conducted by the expedited or full board process. In order for the review to be conducted via the expedited process criteria, such a modification is usually considered a "minor change to previously approved research". Factors that will indicate that a full review is required may include, e.g., involvement of investigators with FCOI, FDA 483 issues that have not been resolved adequately, or any other site-specific issues that are deemed questionable. Additional site amendments (regardless of type of review) do not change the expiration date of the IRB approval for the 'main' protocol.

2. Responsibilities of the SBU Principal Investigator

- Develop a communication plan with the PI's at collaborating sites to ensure they have access to current project status, current protocols, consent documents, etc. regarding the study. The IRB will review the plan provided by the SBU PI to ensure open communication with the collaborating site(s).
- Submit information to the IRB pertaining to the particular characteristics of each site's local research context to be considered through knowledge of its local research context (a) by the IRB, (b) through consultants, or (c) through review by appropriate designated institutional officials at external site(s). Additionally, the submission will also include details for the IRB's evaluation regarding the management plan for information that is relevant to the protection

of participants (e.g., conflict of interest, unanticipated problems involving risks to participants or others, interim results, protocol modifications). When the Stony Brook researcher is the lead researcher of a multi-site study, this information will also be made known to the IRB of record (e.g., Independent IRB).

17.16.4 SBU Ceding IRB Review to an External IRB

Standing Reliance Agreements

SBU has standing agreements in place to engage the services of external IRBs for the review of specific categories of research including:

- Advarra and WCG for industry-initiated, industry-funded research
- NCI's Adult CIRB for NCI research involving adult subjects
- NCI's Pediatric CIRB for NCI research involving children

SBU is a participating institution in the SMART IRB initiative as well, having signed an overarching agreement indicating willingness to cede to other institutions' IRBs, pending satisfactory evaluation of factors identified below. When the SMART IRB agreement is utilized, a letter acknowledging SBU is ceding review is required.

Research that falls within the above parameters must be registered with the University prior to submission to the external IRB following the procedures outlined in Section 17.16.3 (C). Post-approval requirements for investigators are also summarized in Section 17.16.3 (C).
Exception to the pre-registration requirements applies to studies reviewed by NCI-CIRB. These studies may be submitted to the external IRB via the study specific worksheet once other applicable local approvals are in place (i.e. PRC approval). The study may only commence once it is uploaded to myResearch IRB, ancillary reviews are complete, and submission is acknowledged by the ORC.

17.16.4.1 Factors Considered by the ORC in the decision to allow SBU to Cede to an External IRB

SBU may choose to enter into an agreement to rely upon other external IRBs, most commonly when required as a condition of a grant or contract. The Reliance Administrator evaluates the following factors, and others as appropriate, when considering a request to rely upon an external IRB:

1. Phase of the Research. Phase I research will be reviewed by SBU IRB. Exceptions will be considered on a case-by-case basis.
2. The accreditation status of the proposed IRB;
3. The compliance history of the IRB (e.g., outcomes of prior audits or inspections, corrective

actions);
4. Prior experience with the IRB;
5. The federal IRB registration and organizational FWA, as applicable;
6. The expertise and experience of the proposed IRB (e.g., with reviewing the type of research, research procedures, and subject population(s));
7. The research activities to be conducted at the University
8. The risks and complexities of the proposed research;
9. The proposed reliance terms and procedures, including acceptance of SBU local context issues, as well as the procedures for collaborative management of matters such as conflicts of interest disclosures, investigator training, noncompliance, unanticipated problems, and federal reports;
10. The plan for review and allowance of the incorporation of site-specific consent language; and
11. The plan for incorporation of other relevant local requirements or context information in the review process.

When reliance on a non-accredited IRB is proposed, the evaluation will also take into consideration one or more of the following based upon the risks of the research and the University's familiarity with the IRB:

1. A statement of assurance from the proposed IRB that its review will be consistent with applicable ethical and regulatory standards, and that it will report any regulatory investigations, citations, or actions taken regarding the reviewing IRB, and, when applicable, to the organization's FWA (Note, this statement of assurance is acceptable to AAHRPP if the risks are minimal);
2. An attestation about, or summary of, any quality assessment of the reviewing IRB such as evaluation by an external consultant or internal evaluation of compliance using the FDA's self-evaluation checklist or AAHRPP's self-evaluation instrument;
3. The willingness of the external IRB to accommodate requests for relevant minutes and other records of the proposed study and/or to copy the University's HRPP office on correspondence such as determination letters and notices of suspensions or terminations of IRB approval;
4. The willingness of the external IRB to accommodate a request for someone from the relying organization to serve as a consultant to the IRB or to observe the review of the proposed study; and/or
5. An assessment of the external IRB's policies and procedures by the IO or AVP-RC.
6. A non-accredited institution will not be responsible for other additional reviews relevant to the HRPP, including but not limited to biosafety, human stem cell research, conflict of interest, etc. Where SBU IRB completes these reviews, the completed review will be made available to the reviewing IRB.

7. DOD and DOJ sponsored research will not be accepted for reviewed by non-accredited institutions.

The Reliance Administrator will present relevant factors for consideration by the IO or AVP-RC, who will make the final decision regarding whether or not to cede to the requested External IRB. The PI will be notified of the decision.

17.16.5 SBU, External IRB, and SBU Investigator Responsibilities When SBU Cedes Review

1. The External IRB has the same authority as the SBU IRB and all determinations and requirements of the external IRBs are equally binding. See section 17.16.4 for possible exceptions to external IRB vs. SBU responsibilities.
2. Stony Brook University remains responsible for the conduct of the research in which it engages. Research reviewed by external IRBs remains subject to review, acknowledgement, oversight, and monitoring by SBU (in cooperation with the reviewing IRB when appropriate) and must adhere to all applicable policies, procedures, and requirements of the University HRPP. As with SBU IRB-reviewed research, officials of SBU may not approve research that is subject to a reliance agreement if it has not been approved by the reviewing IRB. See section 17.16.4 for possible exceptions to external IRB vs. SBU responsibilities. ORC is responsible for notifying the reviewing IRB when SBU policies that may impact IRB review are updated.

17.16.5.1 Responsibilities of the SBU Investigator When Using an External IRB

General Compliance Requirement:

- The SBU Investigator must be familiar with, and comply with the external IRB's policies and procedures for initial and continuing review, record keeping, prompt reporting, and any additional requirements or procedures outlined in the IRB reliance agreement or companion materials (e.g., reliance SOPs). All information requested by the reviewing IRB must be provided in a timely manner.
- Expectations of PI compliance, as detailed in these SOPs, remain in place regardless of the reviewing IRB.
- Even though the External IRB may be reviewing the study, the study must not begin at SBU until all HSR training, COI disclosure, and required ancillary reviews and certifications (e.g., Chair endorsement, University Hospital sign-offs, IBC, RDRC etc. have been satisfied)
- Relevant ancillary reviews conducted by Stony Brook University will be made available to the reviewing IRB as outlined in the communication plan or Master Service Agreement.

Institutional Registration Requirement:

Studies that will be reviewed by external IRBs must be registered with SBU via myResearch IRB. Details for this registration requirement are available on the SBU website at https://www.stonybrook.edu/commcms/research-compliance/External-IRBs/index.php

The Reliance Administrator will review the information and verify that CITI training, COI review, and any other applicable approvals or requirements have been completed, and determine the need for relaying local context information to the external IRB in accordance with the reliance agreement. Where waivers or alterations of HIPAA authorization are requested, and the external IRB will not be responsible for review (e.g., studies reviewed by the NCI CIRB), the Reliance Administrator will forward such requests to an SBU IRB Chair or a designated expedited reviewer for review. The Reliance Administrator will notify the investigators by e-mail or via myResearch IRB once the proposed research has been cleared for submission to the external IRB. Once approved bythe external IRB, investigators must submit in myResearch IRB a copy of the approval letter, any approved consent document(s), and local recruitment materials. If the protocol was modified during the external IRB review process, the approved version of the protocol should be provided as well.

Post-IRB Approval Requirements:

- Investigators approved through external IRB review must report local unanticipated problems, complaints, and any noncompliance to the ORC via myResearch IRB **in addition to** reporting to the external IRB. Copies of the report submitted to the external IRB are generally acceptable, but additional information may be requested on an as needed basis. External IRB review outcome of reportable events must be provided as soon as it is available.
- Investigators must also submit copies of continuing review reports, updated protocols, updated consent forms, study closures and corresponding IRB approval or acknowledgment. Other documentation must be provided upon request.
- Changes in PI and the addition of other research team members must be submittedto the ORC via the IRB management system prior to the new PI or research team member assuming any study responsibilities. CITI trainings, COI review, and any other applicable requirements will be verified.
    - Notices about, and reports from, DSMB's, external monitors, auditors, or inspectors must be provided to the ORC via the IRB management system.
    - In general, Investigators are reminded that all other University reporting requirements, such as to Compliance, Privacy, and Risk Management, remain applicable in addition to HRPP reporting requirements.

17.16.6 Exceptions to IRB vs. Local Site Responsibilities

Certain areas of responsibility can be handled by either the reviewing IRB or the local site, provided they have been agreed to in the reliance agreement or outlined in a companion document. For example, alternative procedures may be used for any of the following:

1. Conducting and documenting scientific review
2. Management and documentation of ancillary reviews and institutional permissions for research;
3. Training requirements and verification of qualifications and credentials for external investigators and staff;
4. For-cause and not-for-cause compliance reviews;
5. Site-specific consent language
6. HIPAA compliance
7. Handling of matters concerning noncompliance, including which institution is responsible for deciding whether each allegation of non-compliance has a basis in fact, whether an incident of noncompliance constitutes serious or continuing noncompliance, and who will handle reporting to federal agencies
8. Handling of unanticipated problems, and responsibility of reporting to federal agencies when required
9. Review of investigator financial disclosures for COI (note: the reviewing IRB must provide final approval of any management plans generated to mitigate investigator FCOI)
10. Managing organizational conflict of interest relating to the research
11. Procedures for submission and review of interim reports and continuing review materials
12. The communication of IRB determinations and other information to external investigators and organizations
13. In the case of the termination of a reliance agreement, identification of the party responsible for continued oversight of active studies until closure or a mutually agreed upon transfer of the study

17.16.7 NIH Single IRB (sIRB) Policy for Multi-site Research

The NIH sIRB policy applies to grant applications proposing non-exempt multi-site human research which are received for due dates on or after January 25, 2018. For contracts, the policy applies to all solicitations issued on or after January 25, 2018. The policy does not apply to career development, research training, or fellowship awards, nor to sites that are not conducting the same protocol as the other sites (e.g., sites providing statistical support or laboratory analysis only) or to foreign sites.

Exceptions to the policy are automatic when local IRB review is required by federal, tribal, or

state law/regulation/policy. Such exceptions and the basis should be cited in the proposed sIRB plan (see below) and apply only to the site(s) to which the law/regulation/policy applies. Other exceptions will be considered when there is compelling justification. The site(s) and justification for why the site(s) cannot rely on the single IRB of record should be included in the proposed sIRB plan. NIH will consider the exception request and inform the applicant of the outcome.

17.16.7.1 sIRB The Common Rule's Cooperative Research Provision

Effective January 20, 2020, federally funded cooperative research projects that involve more than one domestic institution conducting non-exempt research with human subjects must use a single IRB. The reviewing IRB will be identified by the federal department or agency supporting or conducting the research or propose by the lead institution (subject to the acceptance of the federal department of agency supporting the research). Exceptions to the Requirement include international sites, sites involving tribal nations, or studies that received initial IRB approval prior to January 20, 2020

17.16.7.2 Selection and Designation of a sIRB

SBU investigators submitting applications for NIH-funded multi-site research must describe the sIRB plan in the funding proposal (grant application or contract proposal), and, if applicable, may request direct cost funding to cover additional costs related to the requirements of the NIH policy.

The Reliance Administrator in the ORC **should be contacted as early in the grant writing process as possible** to either confirm that SBU can provide IRB services for the study, or to assist the investigator in making alternative arrangements (e.g., use the IRB at one of the participating sites, ADVARRA IRB, etc.). The Reliance Administrator will consult with others within the organization as needed and make a recommendation to the AVP-RC, or the IO, for

consideration. If SBU IRB can serve as the sIRB, the Reliance Administrator will assist the investigator in working with the Office of Sponsored Programs to ensure accurate, direct cost, budgeting for the service.

Reliance Agreements for sIRB Studies - A Reliance Agreement (or "Authorization Agreement") between the sIRB and the participating sites is required. See Section 17.16.1 for details.

17.16.7.3 sIRB Responsibilities

Per the NIH Policy, the sIRB is responsible for conducting the ethical review of NIH-funded multi-site studies for participating sites and for carrying out the regulatory requirements as specified under the HHS regulations at 45 CFR Part 46.

The sIRB must have the necessary infrastructure to support the required activities (e.g., administrative or regulatory staff, policies, procedures, workflows and technology).

In reviewing multi-site research protocols, the sIRB may serve as a Privacy Board, as applicable, to fulfill the requirements of the HIPAA Privacy Rule for use or disclosure of protected health information for research purposes.

The sIRB can delegate to relying institutions the ability to monitor or observe the conduct of the research and/or the consent process.

The sIRB must review and approve proposed management plans for investigators determined to have a financial conflict of interest.

17.16.7.4 Participating Site Responsibilities

All sites participating in a multi-site study are expected to rely on an sIRB to carry out the functions that are required for institutional compliance with IRB review set forth in the HHS regulations at 45 CFR 46. Participating sites are responsible for meeting other regulatory obligations, such as obtaining informed consent, overseeing the implementation of the approved protocol, and reporting unanticipated problems and study progress to the sIRB. Participating sites must communicate relevant information necessary for the sIRB to consider local context issues and state/local regulatory requirements during its deliberations and must rely on the sIRB to satisfy the regulatory requirements relevant to the ethical review. Although IRB ethical review at a participating site would be counter to the intent and goal of this policy, the policy does not prohibit any participating site from duplicating the sIRB. However, if this approach is taken, NIH funds cannot be used to pay for the cost of the duplicate review.

Additional Responsibilities of the Participating Site:

- Responsibility for reporting incidents of protocol deviations or noncompliance to the sIRB;
- Monitoring or observing the conduct of the research and/or the consent process, when specified in the Reliance Agreement;
- Ensuring disclosure and management of conflicts of interest according to the participating sites' policies and procedures and submit for approval to the sIRB management plans related to investigator FCOI's in human subject research;
- Reporting to the sIRB changes to research implemented to eliminate apparent immediate hazards to participants;
- Ensuring ancillary reviews by University Hospital, IBC, RDRC etc. are conducted prior to commencement of the research (or IRB approval of the research, depending on local policy). When an external IRB serves as the sIRB for a study in which the University is engaged,

investigators must register the study with the University prior to submission to the external IRB following the procedures outlined in Section 17.16.3. Post-approval requirements for investigators are also detailed in Section 17.16.3. Research reviewed by external IRBs remains subject to review, approval, and oversight by SBU and must adhere to all applicable policies, procedures, and requirements required for the safe and ethical conduct of the study.

17.17 Certificates of Confidentiality

Certificates of Confidentiality (CoC) protect research information by prohibiting certain disclosures and conditioning others upon consent from the subject. The protections and requirements of CoCs are outlined in 42 U.S.C. 241(d) and in written policies and requirements of certain Federal agencies such as NIH and CDC and are summarized below.

17.17.1 Definitions

Identifiable, Sensitive Information: means information that is about an individual and that is gathered or used during the course of biomedical, behavioral, clinical, or other research and

1. Through which an individual is identified; or
2. For which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

17.17.2 Protections and Requirements

When a CoC is issued, whether automatically or under an approved application, the person(s) engaged in the research must not disclose or provide the name of a subject or any information, document, or biospecimen that contains identifiable, sensitive information about the subject and that was compiled for the purposes of the research:

1. In any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, unless the disclosure is made with the consent of the individual to whom the information, document, or biospecimen pertains; or
2. To any other person not connected with the research, unless:
    a. Required by Federal, State, or local laws (e.g., adverse event reporting to the FDA, transmissible disease reporting required under State law), but excluding proceedings as described in “1” above;
    b. Necessary for the medical treatment of the subject to whom the information, document, or biospecimen pertains and made with the consent of the subject;

c. Made with the consent of the individual to whom the information, document, or biospecimens pertains; or

d. Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.

17.17.3 Additional Protections

Identifiable, sensitive information protected under a CoC, and all copies thereof, are immune from the legal process, and shall not, without the consent of the of the individual to whom the information pertains, be admissible as evidence or used in any action, suit, or other judicial, legislative, or administrative proceeding.

Identifiable, sensitive information that has been collected under a CoC, and all copies thereof, are protected for perpetuity. If identifiable, sensitive information covered by a CoC is shared with other researchers or organizations, the researchers or organizations must be informed that the information is covered by a CoC and of their responsibility to protect the information accordingly.

Nothing in the rule (42 U.S.C. 241(d)) may be construed to limit the access of a subject to information about himself or herself collected during the research.

When consent is obtained, the consent should inform subjects that a CoC is in place and describe the protections and limitations.

17.17.4 NIH and CDC

The NIH Policy on CoCs applies to *"all biomedical, behavioral, clinical, or other research funded wholly or in part by the NIH, whether supported through grants, cooperative agreements, contracts, other transaction awards, or conducted by the NIH Intramural Research Program, that collects or uses identifiable, sensitive information"* that was commenced or ongoing on or after December 13, 2016.

The CDC requirements for CoCs apply to *"CDC supported research commenced or ongoing after December 13, 2016 and in which identifiable, sensitive information is collected, as defined by Section 301(d)."*

CoCs are automatically granted, and the requirements of such must be complied with, whenever a NIH or CDC funded activity falls within the scope of the NIH policy or CDC's requirements. Investigators and institutions are responsible for determining when research with NIH or CDC support are covered by a CoC.

NIH and CDC expand upon 42 U.S.C. 241(d) by explaining that NIH and CDC consider research in which identifiable, sensitive information is collected or used, to include:

- Human subjects research as defined in 45 CFR 46, including research determined to be exempt (except for exempt research when the information obtained is recorded in such a manner that human subjects cannot be identified or the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects);
- Research involving the collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual;
- Research that involves the generation of individual level, human genomic data from biospecimens, or the use of such data, **regardless of whether the data is recorded in such a manner that human subjects can be identified or the identity of the human subjects can readily be ascertained;** or
- Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual, as defined in subsection 301(d) of the Public Health Service Act.

17.17.5 NIH and CDC CoC Determination

At SBU, the Office of Sponsored Programs will, in consultation with the investigator(s) (or Program or Project Director, if applicable), determine if the NIH policy or CDC requirements applies to research with NIH or CDC involvement or support. The questions outlined in the NIH policy and CDC requirements will be used to guide the analysis.

When it has been determined that the NIH policy or CDC requirements do not apply, investigators (or Program or Project Directors, if applicable) are responsible for consulting with OSP whenever they are proposing changes to the NIH or CDC supported activity that may impact or change the analysis.

The NIH policy and CDC requirements include additional responsibilities and requirements for internal controls and for ensuring that recipients of identifiable, sensitive information protected by a CoC understand that they are also subject to the requirements of subsection 301(d) of the Public Health Service Act.

17.17.6 Application Procedures for non-NIH, non-CDC Research

Any person engaged in human subject research that collects or uses identifiable, sensitive information may apply for a CoC. For most research, CoCs are obtained from NIH. An investigator may apply for a CoC through the NIH Institute or Center funding research in a scientific area similar to the project.

When a researcher is conducting a research project that is covered by the Agency for Healthcare Research and Quality (AHRQ) confidentiality statute (42 U.S.C. section 299c-3(c)), a CoC is not needed (AHRQ notice NOT-HS-18-012). While the AHRQ statute does not define "identifiable", AHRQ applies the PHS Act definition of "identifiable, sensitive information". Investigators should consult with AHRQ when they believe that data might be considered "non-identifiable" or when otherwise uncertain whether a research project falls within the scope of the statute.

When a researcher is conducting a research project that is covered by the Department of Justice (DoJ) confidentiality statute, 28 CFR 22, and/or a NIJ Privacy Certificate, a CoC may not be needed. Investigators should consult with DoJ/NIJ to determine whether a CoC should be obtained.

If there is an Investigational New Drug Application (IND) or an Investigational Device Exemption (IDE), the sponsor can request a CoC from the FDA. When the FDA funds or conducts research, a CoC is automatically issued.

CoCs may also be issued by other Federal agencies and departments, such as SAMSHA and HRSA.

For more information, see the NIH CoC Website.

17.17.7 IRB Review

Investigators are responsible for clearly representing in the IRB submission that a CoC is in place, or that an application for CoC has been submitted or is pending. When the CoC application is in process or pending, the IRB will condition final approval upon its receipt.

For studies that are already underway, investigators must submit an amendment to the IRB, along with updated consent language (if applicable), when a CoC is applied for, or when automatically issued under the NIH policy or CDC requirements.

When reviewing research under a CoC, the IRB will evaluate whether the research plan is consistent with the obligations to protect information and specimens under a CoC and, when consent will be obtained, whether the proposed consent language or other form of notification properly discloses the CoC and appropriately describes the associated protections and limitations. Sample consent language is available on the NIH CoC Website and in the template consent forms available in the IRB electronic management system.

When research is not under a CoC, the IRB may require an investigator to apply for a CoC if the research includes identifiable, sensitive information and the IRB determines that a CoC is necessary to minimize risks and adequately protect subjects' privacy and the confidentiality of subjects' information or specimens.