Rutgers, the State University of New Jersey
Standard Operating Procedures
Human Subject Protection Program

February 2014

Table of Contents

1 Human Subject Protection Program (HSPP)

Rutgers, the State University of New Jersey (Rutgers) fosters a research environment that promotes the respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of the Institution. In the review and conduct of research, actions by the Institution will be guided by the principles (i.e., respect for persons, beneficence, and justice) set forth in the *Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (often referred to as the *Belmont Report*). The actions of Institution will also conform to all applicable federal, state, and local laws and regulations. In order to fulfill this policy, the Institution has established a human subject protections program (HSPP).

1.1 Mission

The mission of the HSPP is to:

- To safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are protected;
- To provide timely and high quality education, review and monitoring of human research projects; and
- To facilitate excellence in human subjects research.

The HSPP includes mechanisms to:

- Establish a formal process to monitor, evaluate and continually improve the protection of human research participants.
- Dedicate resources sufficient to do so.
- Exercise oversight of research protection.
- Educate investigators and research staff about their ethical responsibility to protect research participants.
- When appropriate, intervene in research and respond directly to concerns of research participants.

1.2 Institutional Authority

Rutgers Human Subject Protection Program operates under the authority of the Institution policy 90.2.11 (Policy for Human Subjects Protection and the Institutional Review Board). 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 this policy." The HSPP Policy and these operating procedures are made available to all Rutgers investigators and research staff and are posted on the HSPP website.

1.3 Definitions

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

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

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

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

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

Research as defined by FDA regulations means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. [21 CFR 50.3(c), 21 CFR 56.102(c)]

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

Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act means any activity that evaluates the safety or effectiveness of a device. [21 CFR 812.2(a)]

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

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

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

For research covered by FDA regulations (21 CFR 50 and 56), human subject means an individual who is or becomes a participant in a clinical investigation (as defined below), either as a recipient of the test article or as a control. A subject may be in normal health or may have a medical condition or disease. In the case of a medical device, a human subject/participant also includes any individual on whose tissue specimen an investigational device is used or tested.

Test Article Test articles covered under the FDA regulations include:

a. **Human drugs** – The primary intended use of the product is achieved through chemical action or by being metabolized by the body. A drug is defined as a substance recognized by an official pharmacopoeia or formulary: A substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease; A substance (other than food) intended to affect the structure or any function of the body; A substance intended for use as a component of a medicine but not a device or a component, part or accessory of a device. http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm

b. Medical Devices - A device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them; intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals; or intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its

primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051512.htm

c. Biological Products - include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins. Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues. Biologics are isolated from a variety of natural sources — human, animal, or microorganism — and may be produced by biotechnology methods and other cutting-edge technologies. Gene-based and cellular biologics, for example, often are at the forefront of biomedical research, and may be used to treat a variety of medical conditions for which no other treatments are available.
http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm

d. **Food Additives** - 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.

e. Color Additives - A color additive is any dye, pigment or substance which when added or applied to a food, drug or cosmetic, or to the human body, is capable (alone or through reactions with other substances) of imparting color.
http://www.fda.gov/Food/FoodIngredientsPackaging/ucm094211.htm#foodadd

f. Foods - Foods include dietary supplements that bear a nutrient content claim or a health claim.

g. Infant Formulas – Infant formulas are liquid foods intended for infants which substitute for mother's milk.

Institutional Review Board (IRB) An IRB is a board designated by the Institution to review, to approve the initiation of, and to conduct periodic review of research involving human subjects in research as defined above. 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 Institution.

Institutional Official (IO) The IO is responsible for ensuring that the HSPP at the Institution has the resources and support necessary to comply with all federal regulations and guidelines that govern human subjects research. 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.

Research Under the Auspices of the Institution Research under the auspices of the institution includes research conducted at this institution, conducted by or under the direction of any employee or agent of this institution (including students) in connection with his or her institutional responsibilities, 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.

Engagement Institutions are 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.

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

1.4 Ethical Principles

Rutgers 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:

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

Rutgers Human Subject Protection Program (HSPP), 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 Regulatory Compliance

The HSPP is responsible for ensuring compliance with federal regulations, state law and institutional policies. All human subjects research at Rutgers is conducted in accordance with the policy and regulations found in the Common Rule and 21 CFR 50 and 56. The actions of Rutgers will also conform to all other applicable federal, state, and local laws and regulations.

Research supported by the Department of Defense (DoD) is reviewed and conducted in compliance with part 219 of title 32 CFR, part 980 of title 10 USC, applicable parts of title 21 CFR (50, 56, 312, 600, 812), DoD Instruction 3216.02, DoD Directive 3210.07, and applicable additional requirements from respective DoD component(s). Rutgers has an FWA which is signed by The Institutional Official on behalf of the Institution.

Rutgers voluntarily applies the International Conference on Harmonization ("ICH") Good Clinical Practices ("GCP") Guidelines (sometimes referred to as "ICH-GCP" or "E6") to certain types of human subjects research conducted under its HSPP. In general, Rutgers applies the ICH-GCP guidelines only to the extent that they are compatible with FDA and DHHS regulations. When a sponsor requires institutional ICH-GCP compliance, the IRB will conduct a review in accord with ICH-GCP requirements. See the document "International Conference on Harmonization (ICH) Good Clinical Practices (GCP), Applicability to Human Subjects Research" for guidance on the applicability of the ICH-GCP requirements.

1.6 Federalwide Assurance (FWA)

The federal regulations require that federally funded human subjects research only be conducted at facilities covered by a Federalwide Assurance (FWA) approved by the DHHS Office for Human Research Protections (OHRP). An FWA is an 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 Board that will review and oversee the research, specifies the ethical principles under which the research will be conducted, and names the individuals who will be responsible for the proper conduct of the research.

Rutgers has an OHRP-approved Federalwide Assurance and has appropriately designated IRBs to review all research involving human subjects.

In its FWA, Rutgers has opted to limit the application of the FWA to research funded by DHHS or federal agencies that have adopted the Common Rule.

1.7 Research Covered by the HSPP

Rutgers HSPP covers all research involving human subjects that is under the auspices of the Institution. The research may be externally funded, funded from Rutgers sources, or conducted without direct funding.

1.8 Written policies and procedures

Rutgers 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 Rutgers IRB. This is not a static document. The policies and procedures are annually reviewed and revised by the Chief of the HSPP. The Director of the Office of Research Regulatory Affairs will approve all revisions of the policies and procedures.

The Chief will keep the Institution's research community apprised of new information that may affect the human research protection program, including laws, regulations, policies, procedures, and emerging ethical and scientific issues on its website and through campus electronic mailing lists. The policies and procedures will be available on Rutgers website and copies will be available upon request. Changes to the policies and procedures are communicated to PIs and research staff, and IRB members and IRB staff through global email and HSPP website announcements.

1.9 HSPP Institution

The HSPP is a comprehensive system to ensure the protection of human subjects participating in research. It consists of various individuals and committees such as: the Institutional Official, the Director of Research Regulatory Affairs, the Chief of the HSPP, the campus IRBs, other committees or subcommittees addressing human subjects protection (e.g., Biosafety, Radiation Safety, Radioactive Drug Research, Conflict of Interest), investigators, IRB staff, research staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer) and research pharmacy staff. The objective of this system is to assist the institution 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 HSPP:

1.9.1 Institutional Official

The ultimate responsibility of the HSPP resides with the Associate Vice President for Research Regulatory Affairs who serves as the Institutional Official (IO) of the program. The IO is responsible for ensuring Rutgers HSPP has the resources and support necessary to comply with all institutional policies and with federal regulations and guidelines that govern human subjects research. The IO is legally authorized to represent Rutgers. He/she is the signatory of the FWA and assumes the obligations of the FWA.

The IO also holds ultimate responsibility for:

- oversight of the Institutional Review Board (IRB);
- oversight over the conduct of research conducted by all Rutgers investigators;
- assuring the IRB members are appropriately knowledgeable to review research in accordance with ethical standards and applicable regulations;
- assuring that all investigators are appropriately knowledgeable to conduct research in accordance with ethical standards and applicable regulations;
- oversight of the development and implementation of an educational plan for IRB members, staff and investigators.

1.9.2 Chief of the HSPP

The Chief of the HSPP is selected by and reports to the Director of Research Regulatory Affairs, and is responsible for:

1. Developing, managing and evaluating policies and procedures that ensure compliance with all state, and federal regulations governing research. This includes monitoring changes in regulations and policies that relate to human research protection and overseeing all aspects of the HSPP program.
2. Advising the IO on key matters regarding research at Rutgers.
3. Implementing the institution's HSPP policy.
4. Oversight of the submission, implementation and maintenance of approved FWAs through the Vice President for Research and the Department of Health and Human Services Office of Human Research Protection (OHRP).
5. Managing the finances of Rutgers HSPP.
6. Along with the campus IRB Directors, assisting investigators in their efforts to carry out Institution's research mission.
7. Developing and implementing needed improvements and ensuring follow-up of actions, as appropriate, for the purpose of managing risk in the research program.
8. Developing training requirements as required and as appropriate for investigators, committee members, and research staff, and ensuring that training is completed on a timely basis.
9. Serving as the primary contact at Rutgers for the Office for Human Research Protections (OHRP) of the U.S. Department of Health and Human Services and other federal regulatory agencies.
10. Day-to-day responsibility for the operation of the HSPP office, including supervision of HSPP staff.
11. Responding to faculty, student and staff questions.

12. Working closely with the IRB Director/s on the development of policy and procedures, as well as organizing and documenting the review process.

1.9.3 Institutional Review Board (IRB)

Rutgers maintains appropriately designated IRBs appointed by the Institutional Official (IO). The IRB prospectively reviews and makes decisions concerning all human research conducted at a Rutgers facility, by its employees or agents, or under its auspices. The IRB is responsible for the protection of rights and welfare of human research subjects at Rutgers. It discharges this duty by complying with the requirements of the Common Rule, state regulations, the FWA, and institutional policies.

Rutgers may also utilize the services of external IRB/s; either through a fully executed contract or through a mutually approved Authorization Agreement.

1.9.4 Counsel's Office

Rutgers HSPP relies on the Office of General Counsel for the interpretations and applications of New Jersey law and the laws of any other jurisdiction where research is conducted as they apply to human subjects research.

1.9.5 Department Chairs/Designee (for research conducted at Rutgers Biomedical and Health Sciences)

For those studies conducted at a Rutgers RBHS department, the Department Chairs/designee are responsible for ensuring that the Principal Investigator (PI) is qualified by training and experience to conduct the proposed research. In addition, department chairs are responsible for ensuring that the PI has sufficient resources and facilities to conduct the proposed research. For each protocol submitted to a Rutgers IRB for approval, the department chair must certify that s/he accepts responsibility for assuring adherence to the federal and state regulations and institutional policies governing the protection of human subjects of research, including applicable institutional credentialing requirements.

Department chairs/designees are required to review all proposals before they are submitted to the IRB for review.

Department chairs/designees are responsible for assuring that investigators have the resources required to conduct the research in a way that will protect the right and welfare of participants. Such resources include but are not necessarily limited to personnel, space, equipment and time.

1.9.6 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 for developing 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. 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 completes appropriate training and must obtain all required approvals prior to initiating research. When investigational drugs or devices are used, the investigator is responsible for providing written procedures for their storage, security, dispensing and disposal.

1.9.7 Relationship Among Components

The IRB functions independently of, but in coordination with, other institutional regulatory committees. The IRB, however, makes its 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 subjects regulations.

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 human research that has not been approved by the IRB.

1.9.7.1 Protocol-specific coordination

The Initial Application form, which must be submitted with every protocol, requires PIs to indicate institutional utilization approval, as required, for the research. Examples include, but are not limited to:

The Scientific Review Board

Radiation Safety Committee

Biosafety Committee

ESCRO

University Hospital Office of Clinical Research Administration

Robert Wood Johnson Utilization Group

University Behavioral Health Care

The protocol will be reviewed in the IRB office to ensure that all necessary approvals are included.

1.10 HSPP Operations

In addition to the leadership structure described above, other support staff members for the HSPP include those listed on the current HSPP organizational chart. All HSPP staff must comply with all ethical standards and practices.

1.10.1 HSPP and IRB Offices

The Rutgers HSPP Office reports to the Chief, who has day-to-day responsibilities for its operations.

Additionally, each IRB office is staffed by an IRB Director and/or Assistant Director, and IRB support Staff. The duties and responsibilities for all staff are found in their respective job descriptions, and their performance is evaluated on an annual basis.

1.10.2 IRB Director/Assistant Director

The IRB Director/Assistant Director is responsible for all aspects of the campus IRB throughout the review process of a research proposal involving human subjects. This responsibility includes the initial review of documents and screening of research proposals prior to their review by the IRB, as well as serving as the liaison between the investigators and the IRB. The IRB Director/Assistant Director reviews the IRB minutes for accuracy and ensures proper documentation of discussions, including controverted issues and actions taken by the IRB during its convened meetings.

1.10.3 IRB Support Staff

The IRB Support Staff is responsible for providing administrative and clerical support to the IRB Chair/s and IRB Directors as well as scheduling and coordinating all IRB functions. The IRB Support Staff is also responsible for IRB record retention. The IRB Support Staff is responsible for maintaining complete IRB paper/electronic files, records of all research protocols, and IRB correspondence.

1.11 HSPP Resources

All HSPP/IRB Offices are equipped with all the necessary office, meeting, storage space and equipment to perform the functions required by the HSPP. The adequacy of personnel and non-personnel resources of the HSPP program is assessed on an annual basis by the Director of Research Regulatory Affairs and Chief and are reviewed and approved by the IO.

The Rutgers IO provides resources to the HSPP /IRB Offices, including adequate meeting and office space, and staff for conducting IRB business. Office equipment and supplies, including technical support, file cabinets, computers, internet access, and copy machines, will be made available to the IRB and staff. The resources provided for the HSPP /IRB Offices will be reviewed during the annual budget review process.

1.12 Conduct of Quality Assurance/Quality Improvement Activities

The objective of the Institution's HSPP Quality Assurance/Quality Improvement Plan is to measure and improve human research protection effectiveness, quality, and compliance with Institutional policies and procedures and applicable deferral, state, and local laws. The Quality Assurance/Quality Improvement Plan will be managed and implemented by the Director, HSPP Analysts.

1.12.1 Investigator Audits and Compliance Reviews

Directed ("for cause") audits and routine (not "for cause") compliance reviews will be conducted to assess investigator compliance with federal, state, and local law, and Institution policies, and to identify areas for improvement, and suggest recommendations based on existing policies and procedures. Directed audits of IRB-approved research studies are in response to identified concerns. Routine compliance reviews are conducted using a systematic method to review IRB-approved research on a regular basis. All results will be reported to the Campus Executive/Full IRB board committee.

Activities of auditors during directed audits and routine compliance reviews may include:

a) Confirming that research activities mirror the IRB approved protocol
b) Examining investigator-held research records;
c) Contacting research subjects;
d) Observing research sites where research involving human research subjects and/or the informed consent process is being conducted;
e) Reviewing projects to verify from sources other than the researcher that no unapproved changes have occurred since previous review;
f) Conducting other monitoring or auditing activities as deemed appropriate by the IRBs.

1.12.2 External Site Audits and Compliance Reviews

External directed audits and routine compliance reviews will be conducted at non-Institution sites, where the Institution's IRB serves as the "IRB of Record," to assess compliance with federal, state, and local law, research subject safety, and IRB policies and procedures. These reviews may include items listed in section 1.12.1 above.

1.12.3 Reporting and Disposition

The results of all quality assurance activities are reported to the Principal Investigator and the Chief HSPP. Any noncompliance will be handled according to the procedures of the Institution Human Research Protections Program Policies and Procedures.

If an audit or review finds that subjects in a research project have been exposed to unexpected serious harm, the HSPP Analyst will promptly report such findings to the Chief, who will notify the Director of Research Regulatory Affairs, the IO, the

campus IRB Director and the IRB Chair for immediate action.

1.12.4 HSPP Internal Compliance Reviews

Internal directed audits and random internal reviews of the IRB will be conducted. The results may impact current practices and may require additional educational activities or revisions to SOPs, and will be reported to the Chief and campus IRB Director. The HSPP Analyst will:

a) Review the IRB minutes to determine that adequate documentation of the meeting discussion has occurred. This review will include assessing the documentation surrounding the discussion for protections of vulnerable populations as well as other risk/benefit ratio and consent issues that are included in the criteria for approval;
b. Assess the IRB minutes to assure that quorum was met and maintained;
c) Assess the current reporting process for unanticipated problems;
d) Assess privacy provisions, according to HIPAA; have been adequately reviewed, discussed and documented in the IRB minutes;
e) Evaluate the continuing review discussions to assure they are substantive and meaningful and that no lapse has occurred since the previous IRB review;
f) Observe IRB meetings or other related activities;
g) Review IRB files to assure retention of appropriate documentation and consistent Institution of the IRB file according to current policies and procedures;
h) Review the IRB database/electronic system to assure all fields are completed accurately;
i) Review reviews by the IRB members;
j) Verify IRB approvals for collaborating institutions or external performance sites;
k) Review the appropriate metrics (for example, time from submission to first review) to evaluate the quality, efficiency, and effectiveness of the IRB review process;
l) Review IRB member rosters and training records.
m) Other monitoring or auditing activities deemed appropriate by the IRB.

The Chief will review the results of internal reviews with the campus IRB Directors. If any deficiencies are noted in the review, a corrective action plan will be developed by the Director and approved by the Chief. The campus IRB Directors will have responsibility for implementing the corrective action plan, the results of which will be evaluated by the HSPP Chief.

1.12.5 Quality Improvement

All quality assurance reports, both research-related and HSPP-related, will be reviewed by the Chief in collaboration with either the campus IRB Directors and/or the Director of Research Regulatory Affairs in order to determine if systemic changes are required in the HSPP to prevent re-occurrence. If so, a corrective action plan will be developed, implemented and evaluated.

1.13 Collaborative Research Projects

In the conduct of cooperative research projects, Rutgers acknowledges that each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with applicable federal regulations. When a cooperative agreement exists, Rutgers may enter into a joint review arrangement, rely on the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort. A formal relationship must be established between the Rutgers and the other institution through either an Authorization Agreement or a Memorandum of Understanding. This relationship must be formalized before the Rutgers IRB will accept any human research proposals from the other institution or rely on the review of the other institution.

It is the policy of Rutgers to assure that all facilities participating in a human subjects study receive adequate documentation about the study in order to protect the interests of study participants. Before a study can begin, it must be approved by the IRBs of record for each participating facility and, where appropriate, the IRB of record for the coordinating facility.

For collaborative research, the PI must identify all institutions participating in the research, the responsible IRB(s), and the procedures for dissemination of protocol information (IRB initial and continuing approvals, relevant reports of unanticipated problems, protocol modifications, and interim reports) between all participating institutions.

When Rutgers relies on another IRB, the Chief of the HSPP Office and campus IRB Director will review the policies and procedures of the IRB to ensure that they meet Rutgers standards. If the other institution holds a FWA, it will be assumed that Rutgers standards are being met.

When Rutgers reviews research conducted at another institution, the particular characteristics of each institution's local research context must be considered, either (i) through knowledge of its local research context by the Rutgers IRB or (ii) through subsequent review by appropriate designated institutional officials, such as the Chairperson and/or other IRB members.

If Rutgers is the coordinating facility the Principal Investigator must document how the important human subject protection information will be communicated to the other participating facilities engaged in the research study. The investigator is responsible for serving as the single liaison with outside regulatory agencies, with other participating facilities, and for all aspects of internal review and oversight procedures. The investigator is responsible for ensuring that all participating facilities obtain review and approval from their IRB of record and adopt all protocol modifications in a timely fashion. The investigator is responsible for ensuring that the research study is reviewed and approved by any other appropriate committees at the coordinating facility and at the engaged facilities prior to enrollment of participants.

The PI must follow these procedures when Rutgers is the coordinating facility:

- During the initial IRB submission of the multi-site study, the investigator indicates in writing on the application form or in an application letter that Rutgers is the coordinating facility of a multi-site study.
- The investigator submits the following information in their IRB application materials:
    - Whether research activities at participating institutions are defined as engagement
    - Name of each participating facility
    - Confirmation that each participating facility has an FWA (including FWA number)
    - Contact name and information for investigator at each participating facility
    - Contact name and information for IRB of record at each participating facility
    - Method for assuring all participating facilities have the most current version of the protocol
    - Method for confirming that all amendments and modifications in the protocol have been communicated to participating sites
    - Method for communicating to participating facilities any serious adverse events and unanticipated problems involving risks to subjects or others
    - Method of communicating regularly with participating sites about study events
- The investigator submits approval letters from all the IRB of record for all participating sites.
- The investigator maintains documentation of all correspondence between participating sites and their IRBs of record.

When Rutgers is engaged in only part of a cooperative research project, the Rutgers IRB only needs to approve the part(s) of the research in which the Rutgers investigator is engaged. For example, if Rutgers is operating the statistical center for a multicenter trial that receives identifiable private information from multiple other institutions, the Rutgers IRB reviews and approves the research activities related to the receipt and processing of the identifiable private information by the statistical center.

2 Institutional Review Board

Rutgers has established Institutional Review Boards (IRBs) to ensure the protection of human subjects in human subjects research conducted under the auspices of the Institution. All non-exempt human subjects research conducted under the auspices of the Institution must be reviewed and approved by a Rutgers IRB prior to the initiation of the research.

Although Rutgers has authorized a number of IRBs to fulfill this function, all campus IRBs follow the same policies and procedures. Therefore, for the purposes of this document, all campus IRBs will be referred to as Rutgers IRB.

Rutgers also utilizes the services of non-Rutgers IRBs. They include (but are not limited to):

- Western IRB: the WIRB option is available to Rutgers investigators who conduct industry-initiated, industry-sponsored research activities in which all activities are conducted at Rutgers sites and by Rutgers personnel.
- NCI's Adult CIRB: for applicable cooperative oncology group protocols involving adult subjects
- NCI's Pediatric CIRB: for applicable cooperative oncology group protocols involving minor subjects.

The authorized non-Rutgers IRBs that serve as the IRB-of-record for Rutgers have the same authority as the campus IRBs and all determinations and findings of the non-Rutgers IRBs are equally binding on all research under the auspices of the institution. Procedures for the non-Rutgers IRBs are found in Section 3.16.

The following describes the authority, role and procedures of the campus IRB.

2.1 IRB Authority

The IRB derives its authority from Rutgers Policy 90.2.11. Under the Federal Regulations, the IRBs authority includes:

1. To approve, require modifications to secure approval, or disapprove all research activities overseen and conducted under the auspices of Rutgers;
2. To suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to participants;
3. To observe, or have a third party observe, the consent process; and
4. To 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. Rutgers Administration officials may

strengthen requirements and/or conditions, or add other modifications to secure Administrative approval or approval by another Administrative oversight committee. Previously approved research proposals and/or consent forms must be re-approved by the IRB before initiating the changes or modifications.

2.2 Number of IRBs

The IO, the Director of Research Regulatory Affairs, the Chief of the HSPP Office, and the campus IRB Director will review the activity of the campus IRBs on at least an annual basis and make a determination as to the appropriate number of IRBs committees that are needed for the institution. This determination will be based on the evaluation of the performance of IRB.

2.3 Roles and Responsibilities

2.3.1 Chair of the IRB

The Rutgers Institutional Official (IO) appoints a Chair of the IRB to serve for a mutually agreed upon term. Any change in appointment, including reappointment or removal, requires written notification by the IO.

The IRB Chair should be a highly respected individual, from within Rutgers, 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 fall primarily on the shoulders of the Chair. The IRB must be perceived to be fair, impartial and immune to pressure by the institution's administration, the investigators whose protocols are brought before it, and other professional and nonprofessional sources.

The IRB Chair is responsible for conducting the meetings and is a signatory for correspondence generated by the IRB.

The IRB Chair may designate other IRB members or staff to perform duties, as appropriate, for review, signature authority, and other IRB functions, e.g., the Vice Chair and Director of the campus IRB office.

The IRB Chair advises the Institutional Official, the Director of Research Regulatory Affairs, the Chief of the HSPP Office and the campus IRB Director about IRB member performance and competence.

The performance of IRB Chair will be reviewed on an annual basis by the Director of Research Regulatory Affairs, the Chief of the HSPP Office in consultation with the Institutional Official and campus IRB Director. Feedback from this evaluation will be provided to the Chair. If the 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 Chair, he/she may be removed.

2.3.2 Vice Chair of the IRB

The Vice Chair/s serves as the Chair of the IRB in the absence of the Chair and has the same qualifications, authority, and duties as Chair.

2.3.3 Subcommittees of the IRB

The IRB Chair, in consultation with the campus IRB Director and/or the IRB committee may designate one or more other IRB subcommittees of the IRB to perform duties, as appropriate, to review and undertake other IRB functions, and to make recommendations to the IRB for Research that is not Expedited. The IRB Chair, in consultation with the campus IRB Director and/or the IRB committee, 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). Members of the IRB Subcommittee must be experienced members of the IRB, and should be matched as closely as possible with their field of expertise to the study assigned to the IRB Subcommittee.

2.4 IRB Membership

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 Rutgers. Rutgers has procedures that specifically outline the requirements of protocol review by individuals with appropriate scientific or scholarly expertise.

In addition, the IRB will include members who are knowledgeable about and experienced working with vulnerable populations that typically participate in Rutgers research.

Individuals from Rutgers Administrative offices and affiliate institutions may not serve as voting 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/ex officio members.

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. A member of the IRB may fill multiple membership position requirements for the IRB.

2.5 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 institution.
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.
3. 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 institutional policies and regulations, applicable law, and standards of professional conduct and practice. The IRB will therefore include persons knowledgeable in these areas.
4. If the IRB regularly reviews research that involves a vulnerable category of subjects (e.g., children, prisoners, pregnant women, or handicapped or mentally disabled persons), consideration will be given to the inclusion of one or more individuals on the IRB, who are knowledgeable about and experienced in working with these subjects. When protocols involve vulnerable populations, the review process will include one or more individuals who are knowledgeable about or experienced in working with these participants, either as members of the IRB or as consultants.
5. 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. The IRB shall not consist entirely of members of one profession.
6. 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.
7. The IRB includes at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.
8. The IRB includes at least one member who represents the general perspective of subjects.
9. One member may satisfy more than one membership category.
10. The Chief HSPP, campus IRB Directors, and personnel of Rutgers HSPP or IRB Office may be voting members of the IRB.

On at least an annual basis, the IRB Chairs and the campus IRB Director/s shall review the membership and composition of the IRBs to determine if they continue to meet

regulatory and Institutional requirements. Required changes in IRB membership will be reported to the OHRP.

2.6 Appointment of Members to the IRB

The IRB Chair, Vice Chair, the Director or Research Regulatory Affairs, the Chief of the HSPP Office, and/or the campus IRB Director may identify a need for a new, replacement, or alternate member. Members will be solicited from within the university and from the communities surrounding the Rutgers campuses.

The campuses IRB Director/s receive nominations and volunteer requests to serve on the campus IRBs.

Faculty and Staff

Rutgers Department Chairs or Managers may nominate faculty and staff to serve on the IRB or the IRB Director or Chair may approach Department Chairs and/or Managers to request certain individuals for membership.

Students

Students if nominated to serve on the IRB must have appropriate school approval.

Un-affiliated IRB Members (Community Members)

Un-affiliated members may be nominated by anyone and considered for membership based on local context.

The final appointment is made by the Institutional Official, in consultation with, the IRB Chair and the campus IRB Director.

Appointments are made for an agreed upon period of service. Any change in appointment, including reappointment or removal, requires written notification. Members may resign by written notification to the Chair.

On an annual basis, the IRB Chair and the campus IRB Director reviews the membership and composition of the IRB to determine if they continue to meet regulatory and institutional requirements.

2.7 Alternate members

The appointment and function of alternate members is the same as that for primary 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 the 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.

2.8 IRB Member Conflict of Interest

No IRB member may participate in the review (initial, continuing, or modification) of any research project in which the member 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 recuse him/herself from the deliberations and vote by leaving the room.

IRB members may find themselves in any of the following conflicts of interest when reviewing research:

1. Where the member or consultant is involved in the design, conduct, and reporting of the research.
2. Where an immediate family member of the member or consultant is involved in the design, conduct, and reporting of the research.
3. Where the member holds significant financial interests related to the research being reviewed
4. 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 conflicting interest are excluded from being counted towards quorum. All recusals by members with COI are recorded in the minutes.

2.9 Use of Consultants

When necessary, the IRB Chair or the campus IRB Director may solicit individuals from within Rutgers or the community with 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 an outside reviewer is determined in advance of the meeting by the Director or the Chair by reviewing the protocols scheduled to be reviewed at the convened meeting. The campus IRB Office will ensure that all relevant materials are provided to the outside reviewer prior to the convened meeting.

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 protocol.

The campus IRB Director reviews the conflicting interest policy for IRB members with consultants and consultants must verbally confirm to the IRB that they do not have a conflict of interest prior to review. Individuals who have a conflicting interest or whose spouse or family members have a conflicting interest in 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 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 researcher'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).

2.10 Duties of IRB Members

The agenda, submission materials, protocols, proposed informed consent forms and other appropriate documents are distributed to members prior to the convened meetings at which the research is scheduled to be discussed. Members will review the materials approximately one week before each meeting, in order to participate fully in the review of each proposed project. IRB members will treat the research proposals, protocols, and supporting data confidentially. All paper copies of the protocols and supporting data can be returned to the IRB staff at the conclusion of the IRB meeting for professional document destruction.

2.11 Attendance Requirements

Members should attend all meetings for which they are scheduled. If a member is unable to attend a scheduled meeting, they should inform the campus IRB office. If the inability to attend will be prolonged, a request for an alternate to be assigned may be submitted to the Chair or the Director.

If an IRB member is to be absent for an extended period of time, such as for a sabbatical, he or she should 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 if the member is not returning to the IRB. If the member has a designated alternate the alternate can serve during the primary member's absence, provided the IRB has been notified in advance.

2.12 Training / Ongoing Education of Chair and IRB Members in Regulations, Procedures

A vital component of a comprehensive human research protection program is an education program for IRB Chair and the IRB members. Rutgers is committed to

providing training and an on-going educational process for IRB members and the staff of the IRB and HSPP Offices, related to ethical concerns and regulatory and institutional requirements for the protection of human subjects.

Orientation

New IRB members, including alternate members will meet with the campus IRB Director or Assistant Director for an informal orientation session. At the session, the new member will be given an IRB packet that includes the following documents or electronic links to:

- Belmont Report;
- Rutgers Policies and Procedures for the Protection of Human Subjects;
- Federal regulations relevant to the IRB
- *IRB Member Handbook*
- Pertinent forms and templates

New members are required to complete the Initial Education requirement for IRB members before they may serve as a reviewer.

Initial Education

IRB members will complete the required modules in the CITI Course in the Protection of Human Research Subjects, including the IRB Member Module - "What Every New IRB Member Needs to Know."

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.

In addition to initial training requirements, IRB members and staff must also satisfy continuing education requirements. Rutgers uses the following activities as a means for offering continuing education to IRB members and staff:

- In-service training at IRB meetings;
- Training workshops;
- Copies of appropriate publications;
- Identification and dissemination by the Director of new information that might have affected 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 members and staff are also required to complete CITI training every 3 years as part of the Rutgers continuing education requirements.

Members and staff who are unable to attend education sessions will be provided with the opportunity to make-up any training that they missed. If a make-up session is not possible (e.g. a webinar or conference), then an equivalent educational opportunity will be offered at the discretion of the Director.

The activities for continuing education vary on a yearly basis depending on operating budget and areas of need, as determined by the Chief and campus IRB Directors. The Chief determines which continuing education activities are mandatory for IRB members and staff in a given year and the IRB office tacks whether each individual has satisfied the requirements. IRB members who have not fulfilled their continuing education requirements may not be allowed to attend IRB meetings until they are fulfilled. Continuing noncompliance may result in the individual not being renewed as an IRB member

The HSPP Office Professional Staff is required to complete the entire CITI Course in the Protection of Human Research Subjects.

2.13 Liability Coverage for IRB Members

Rutgers insurance coverage applies to employees and any other person authorized to act on behalf of Rutgers or acts or omissions within the scope of their employment or authorized activity.

2.14 Review of IRB Member Performance

The IRB Members' performance will be reviewed on an annual basis by the Chief, campus IRB Director in consultation with the IRB Chair. IRB members will receive formal feedback on the results of this review.

The IRB Chair in consultation with the IRB Director will extend either a written invitation for membership renewal or a membership-term conclusion letter at the end of their term.

The IRB Chair in consultation with the IRB Campus Director and Chief HSPP may remove a member at any time.

Membership renewals and removals will be based on the following criteria:

1. IRB meeting attendance
2. Number and/or quality of IRB reviews (both expedited and full board)
3. Conduct during IRB meetings
4. Attendance at on-going educational activities

2.15 Reporting and Investigation of Allegations of Undue Influence

If an IRB chair, member, or staff person feels that the IRB has been unduly influenced by any party, they shall make a confidential report to the Director of Research

Regulatory Affairs, the Chief, or the Institutional Official (IO), depending on the circumstances. The official receiving the report will conduct a thorough investigation and corrective action, if indicated, will be taken to prevent additional occurrences.

3 IRB Review Process

All human subjects research conducted under the auspices of Rutgers 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 Rutgers IRB.

3.1 Definitions

Administrative Closure: An administrative closure is a notation of the IRB that a study's IRB approval has expired and the PI has been non-responsive in seeking any continuing approval.

Administrative Withdrawal: An Administrative withdrawal is when an administrator withdraws a protocol file, which the submission was received by the IRB and assigned a protocol number but was not acted upon by the committee due to a request or lack responsive of the PI.

Minimal Risk: Minimal risk means that 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.

Minor Change: A minor change is one which, in the judgment of the IRB reviewer, makes no substantial alteration in:

1. the level of risks to subjects
2. the research design or methodology (adding procedures that are not eligible for expedited review [See Section 3.5] would not be considered a minor change)
3. the number of subjects enrolled in the research (no greater than 10% of the total requested)
4. the qualifications of the research team
5. the facilities available to support safe conduct of the research
6. any other factor which would warrant review of the proposed changes by the convened IRB.

Quorum: A quorum of the IRB 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 scientist must be included in the quorum.

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

Termination of IRB approval: A termination of IRB approval is 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.

3.2 IRB Actions

The IRB will render decisions on research activities and may make one of the following determinations:

Approved

The research activity, as submitted, meets the criteria for approval as defined in 45 CFR46.111 (and 21 CFR 56.111, if applicable).

- ☐ The date of approval is the date on which the IRB reaches an approval determination.
- ☐ The investigator will not begin research activities until he/she has received the written IRB notification of approval.

Approved with Conditions – (Research Activities Cannot Begin)

To secure approval, the IRB requires modifications in the research or other action(s) to be taken by the Investigator.

Examples:

- Submission of the signed Financial Disclosure Form
- Completion of CITI training
- Revised Research Protocol
- Clarification of information provided in the application
- Revised language to be incorporated into consent documents
- Conflict of Interest Determination

The IRB will include in its written notification of deferral, a statement of the reasons for its decision and give the Investigator an opportunity to respond.

- ☐ New Application: The application may be revised and resubmitted for reconsideration by the IRB **or** the Investigator may provide justification to the IRB why the actions or changes are unnecessary.

- The investigator will take the actions, make the requested changes, and/or justify in the deferral response why the actions or changes are unnecessary before the IRB will reconsider the application.
- The investigator will include a copy of any revised documents including protocol and consent form with their deferral response.
- The investigator will not begin the research activities until he/she receives written notification of approval from the IRB.
- The date of approval is the date on which the IRB reaches an approval determination.

☐ Modification(s): The modification(s) cannot be implemented and the IRB expects the research will continue as previously approved.

- The investigator will continue to conduct the research activities as previously approved by the IRB.
- The investigator will take the actions, make the requested changes and/or justify in the response why the actions and/or changes are unnecessary before the IRB will reconsider the application.
- The investigator will include a copy of any revised documents including protocol and consent form with their deferral response.
- The investigator will not implement proposed modifications until he/she receives written notification of approval from the IRB.
- The date of approval is the date on which the IRB reaches an approval determination.

☐ Continuing Review:

- The investigator will take the actions, make the requested changes and/or justify why the changes are unnecessary before the IRB will reconsider the application.
    - ❖ ☐ If the Continuing Review has not been approved by the expiration date, IRB approval will expire and the Investigator must proceed in accordance with Expired IRB procedures.
- The investigator will include a copy of any revised documents including protocol and consent form with their response.
- The investigator will not continue the research activities beyond the expiration date until they have received the written notification of approval from the IRB.
- The date of approval is the date on which the IRB reaches an approval

Approved with Stipulations (Research Activities May Begin with Stipulated Limitations)

The IRB has approved the proposed research or changes as submitted with **stipulations.** Stipulations mandated by the IRB may prohibit the investigator(s) from conduction or initiating certain aspects of the study. Stipulations may only be removed by submitting the required documents for review by the IRB.

> Example:
> For Multisite studies where Rutgers is the coordinating center - Research at other institutions may not begin until IRB approval received from that institution

Disapproved

The IRB has determined that the research activity, as submitted, does not meet the criteria for approval as defined in 45 CFR 46.111 (and 21 CFR 56.111, if applicable) and/or that the IRB requires substantial revisions to the application, informed consent document(s), or other relevant documents in order to assess the subject's risk/benefit ratio.

If the IRB disapproves a research activity, it will include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing, at the discretion of the IRB.

☐ Disapproved New Application:

- The application may be reconsidered as a new submission after substantial changes have been made to the study.

☐ Disapproved Modification(s):

- The change cannot be implemented, and the IRB expects the research will continue as previously approved.

The investigator will not conduct any research activities that have been disapproved in writing by the IRB.

Tabled/Deferred

An application may be tabled for the following reasons:

- Lack of meeting time to conduct thorough review of the item
- Loss of quorum
- Insufficient information to make a determination
- Other reasons as determined by the Chairperson
- The application will be placed on a future IRB agenda

☐ The application will be placed on a future IRB agenda

The investigator will not initiate any new research activities or implement proposed

changes to previously approved research until the application has subsequently been reviewed by the IRB and they have received written notification of IRB approval.

3.3 Human Subjects Research Determination

The investigator is responsible for the initial assessment as to whether an activity constitutes human subjects research. The investigator should make this assessment based on the definitions of "human subject" and "research" in Section 1.3. Since the Institution will hold them responsible if the determination is not correct, investigators are advised to request a confirmation that an activity does not constitute human subjects research from the IRB Office. The request may be made through a formal written communication. All requests must include sufficient documentation of the activity to support the determination.

Determinations as to whether an activity constitutes human subjects research will be made according to the definitions in Section 1.3 using the Human Subjects Research Determination Decision Tree. Determinations regarding activities that are either clearly or clearly not human subjects research (i.e. non-human subject, QA/QI projects or Program Evaluations and Classroom-directed exercises), based on the checklist, may be made by the designated IRB staff. Determinations regarding less clear-cut activities will be referred to the IRB Chair or designee, who may make the determination or refer the matter to the full IRB.

Documentation of all determinations made through the IRB Office will be recorded and maintained in the IRB Office. Formal submissions will be responded to in writing and a copy of the submitted materials and determination letter/email will be kept on file.

3.4 Exempt Studies

All research using human subjects must be approved by the Institution. Certain categories of research (i.e., "exempt research") do not require convened IRB review and approval. Exempt research is subject to institutional review and must be determined and approved by the IRB Chair or designee.

3.4.1 Limitations on Exemptions

Children: Exemption 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.

Prisoners: Exemptions do NOT apply. IRB review is required**.**

3.4.2 Categories of Exempt Research

With the above exceptions, research activities not regulated by the FDA (see Section 3.3.3 for FDA Exemptions) in which the only involvement of human subjects will be in one or more of the following categories are exempt from IRB review, but require institutional review, at Rutgers :

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as
    a) research on regular and special education instructional strategies, or
    b) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
    a) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
    b) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject’s financial standing, employability, or reputation.
3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2), if:
    a) the human subjects are elected or appointed public officials or candidates for public office; or
    b) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.
4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

    NOTE: In order to be eligible for this exemption, all of the materials have to exist at the time the research is proposed.
5. Research and demonstration projects which are conducted by or subject to the approval of federal department or agency heads, and which are designed to study, evaluate, or otherwise examine:
    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.

e) The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older American Act).

f) The research demonstration project must be conducted pursuant to specific federal statutory authority, there must be no statutory requirements of IRB review, the research must not involve significant physical invasions or intrusions upon the privacy of subjects', and the exemption must be invoked only with authorization or concurrence by the funding agency.

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

   a) If wholesome foods without additives are consumed; or

   b) 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.

3.4.3 FDA Exemptions

The following categories of clinical investigations are exempt from the requirements of 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 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. [21 CFR 56.104(d)]

3.4.4 Procedures for Exemption Determination

In order to obtain an exemption determination investigators must complete and submit:

1. a completed **Initial Application**;
2. all recruitment materials (e.g., letter of invitation, recruitment script, flyer),
3. consent form (when appropriate) or request for waiver of consent
4. all surveys, questionnaires, instruments, etc.,

5. IRB approval or appropriate letter(s) of permission from each non-Rutgers site of performance
6. if sponsored, one copy of the grant application(s) and/or contract
7. verification of current human research protection training for all members of the research team, including the faculty advisor
8. Investigator Financial and other personal interests disclosure form (for RBHS studies).

The IRB Chair (or designee) reviews all requests for exemptions and determines whether the request meets the criteria for exempt research. The IRB Chair may designate an IRB member/s to review requests for exemptions submitted to the IRB. The Chair selects designees who are qualified to review this category of submission based on their expertise of the protocol content and knowledge of regulations pertaining to research. If there is not a designated reviewer to consider requests for exemptions, the IRB Chair reviews the requests. Individuals involved in making the determination of an IRB exempt status of a proposed research project cannot be involved in the proposed research. Reviewers do not have any apparent conflict of interest.

To document the reviewer's determination of the request for exempt research, he/she completes the exemption determination form. The reviewer verifies on the form whether the submission meets the definition of human subjects research (See Section 1.3). If the request meets the definition of human subject research, the reviewer indicates whether the request for exemption was approved or denied, and if approved, the rationale for the determination and category under which it was permitted.

Investigators will be informed via written communication as to the determination of exempt status.

Exempt studies are communicated to the IRB at a convened meeting within approximately one month of the approval of the exemption

3.4.5 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 (i.e. informed consent) for subjects in keeping with the guidelines of the Belmont Report.

3.5 Expedited Review

An IRB may use the expedited review procedure to review either or both of the following:

1. some or all of the research appearing on the list of categories of research eligible for expedited review and found by the reviewer(s) to involve no more than minimal risk,

2. minor changes in previously approved research during the period (of one year or less) for which approval is authorized

3.5.1 Categories of Research Eligible for Expedited Review

The categories of research eligible for expedited review were published in a Federal Register notice 63 FR 60364-60367, November 9, 1998.

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 categories in this list apply regardless of the age of subjects, except as noted.

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.

The expedited review procedure may not be used for classified research involving human subjects.

The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.

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

(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, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 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 8 week period and collection may not occur more frequently than 2 times per week. [Children are defined in the DHHS regulations as "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."][45 CFR 46.402(a)]

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

Examples: (a) hair and nail clippings in a nondisfiguring 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) uncannulated 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 nonresearch 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) and (b)(3). This listing refers only to research that is not exempt.]

(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; *or*
>
> (b) where no subjects have been enrolled and no additional risks have been identified; *or* (c) where the remaining research activities are limited to data analysis.

[Of note, category (8) identifies three situations in which research that is greater than minimal risk and has been initially reviewed by a convened IRB may undergo subsequent continuing review by the expedited review procedure.

For a multi-center protocol, an expedited review procedure may be used by the IRB at a particular site whenever the conditions of category (8)(a), (b), or (c) are satisfied for that site. However, with respect to category 8(b), while the criterion that "no subjects have been enrolled" is interpreted to mean that no subjects have ever been enrolled at a particular site, the criterion that "no additional risks have been identified" is interpreted to mean that neither the investigator nor the IRB at a particular site has identified any additional risks from any site or other relevant source.]

(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 IRB.]

3.5.2 Expedited Review Procedures

Under an expedited review procedure, the review may be carried out by the IRB Chair or by one or more reviewers designated by the Chair from among members of the IRB. IRB members who serve as designees to the IRB Chair for expedited review will be matched as closely as possible with their field of expertise to the study.

The Chair will designate IRB members eligible to conduct expedited review. The IRB Staff will select expedited reviewers from that list. Selected reviewers will have the qualifications, experience and knowledge in the content of the protocol to be reviewed, as well as be knowledgeable of the requirements to approve research under expedited review. IRB members with a conflict of interest in the research will not be selected.

When reviewing research under an expedited review procedure, the IRB Chair, or designated IRB member(s), should receive and review all documentation that would normally be submitted for a full-board review including the complete protocol, a Continuation review form summarizing the research since the previous review (including modifications and unanticipated problems), notes from the pre-screening conducted by the IRB Office staff, the current consent documentation and determine the regulatory criteria for use of such a review procedure by using the Expedited review determination form.

If the research meets the criteria allowing review using the expedited procedure, the reviewer(s) conducting initial or continuing review complete the appropriate review form checklist (Initial Protocol Review Form or Continuing Review Form) to determine whether the research meets the regulatory criteria for approval. If the research does not meet the criteria for expedited review, then the reviewer will indicate that the research requires full review by the IRB and the protocol will be placed on the next agenda for an IRB meeting.

In reviewing the research, the reviewers will follow the Review Procedures and may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth below.

Reviewers will indicate approval, required modifications or requirement for convened board review on the protocol review/initial review form and submit to the IRB Office. If

modifications are required, the IRB Office staff will inform the investigator through written communication.

In the event that expedited review is carried out by more than one IRB member and the expedited reviewers disagree, the IRB Director and/or IRB Chair may make a final determination. Upon the discretion of the IRB Director or IRB Chair the protocol will be submitted to the fully convened IRB for review.

3.5.3 Informing the IRB

Members of the IRB will be apprised of all expedited review approvals by means of a list in an agenda within approximately one month of the expedited approval. Any IRB member can request to review the full protocol by contacting the IRB Office if the study is not included in the eIRB system

3.6 Convened IRB Meetings

Except when an expedited review procedure is used, 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.

3.6.1 IRB Meeting Schedule

The IRB meets on a regular basis throughout the year. The schedule for the IRB may vary due to holidays or lack of quorum. The IRB meeting schedule and submission deadlines for each campus shall be posted on the HSPP website. Special meetings may be called at any time by the IRB Chair or the IRB Director.

3.6.2 Preliminary Review

The IRB staff may perform a preliminary administrative review of all protocol materials submitted to the IRB Office for determination of completeness and accuracy, including an informed consent checklist. Only complete submissions will be placed on the IRB agenda for review. The investigator will be informed either by e-mail, phone or in person of missing materials and the necessary date of receipt for inclusion on that month's agenda. In the case of a PI who is submitting a protocol for the first time or an investigator who may not be well-versed in the protocol submission procedures, individualized IRB consultations can be arranged. Specific questions about the IRB policies and procedures, determination of whether a particular protocol is human research or not and what particular forms are required for a particular study can be submitted in writing to the IRB staff for information and/or clarification. Individual appointments with the IRB staff can also be arranged and are strongly recommended for first-time submissions.

3.6.3 Primary and Secondary Reviewers

After it has been determined that the protocol submission is complete, the IRB staff, with the assistance of the IRB Director or Assistant Director will assign protocols for

review paying close attention to the scientific content of the protocol, the potential reviewer's area of expertise and representation for vulnerable populations involved in the research. A primary and, if appropriate, a secondary reviewer will be assigned to each protocol. A reviewer may be assigned several protocols or other research items for review (i.e. reportable events). Reviewers are assigned to all protocols requiring initial review, continuing review, and modifications. When the IRB is presented with a protocol which may be outside of the knowledge base or representative capacity of all of the IRB members, an outside consultant will be sought. Protocols for which appropriate expertise cannot be obtained for a given meeting will be deferred to another meeting when appropriate expertise can be achieved.

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, an absent reviewer can submit their written comments for presentation at the convened meeting.. It should be noted that all of the IRB members receive and is expected to review all studies, not just the ones they are responsible for reviewing.

3.6.4 Pre-Meeting Distribution of Documents

All required materials need to be submitted (in full) by the posted deadlines prior to the convened meeting for inclusion on the following IRB agenda. The meeting agenda will be prepared by the IRB office staff under the supervision of the IRB Director and distributed to the IRB members prior to the meeting. All IRB members receive their review materials which include the IRB agenda, prior month's meeting Minutes, applicable business items and audits, appropriate continuing education materials and protocol review materials approximately 5 business days before the scheduled meeting to allow sufficient time for the review process. Exceptions to this deadline may be made at the discretion of the Chair or designee.

3.6.5 Materials received by the IRB

Each IRB member receives and reviews the following documentation, as applicable, for all protocols on the agenda:

- Complete Protocol Application form
- Proposed Consent / Parental Permission / Assent Form(s)
- Recruitment materials / subject information

- Data collection instruments (including all surveys and questionnaires)

At least one reviewer must receive and 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).

Any IRB member may request any of the materials by contacting the IRB Office.

If an IRB member requires additional information to complete the review they may contact the investigator directly or may contact the IRB Office to make the request of the investigator.

Protocol reviewers will use a review checklist/s as a guide to completing their review.

3.6.6 Quorum

A quorum consists of a simple majority (more than half) of the voting membership on the roster, 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 scientist must be included in the quorum.

At meetings of the IRB, a quorum must be established and maintained for the deliberation and vote on all matters requiring a vote. 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 Chair, with the assistance of the IRB staff, will be responsible to ensure that the IRB meeting remains appropriately convened. If a quorum is not maintained, the pending action item must be deferred or the meeting terminated. The IRB Staff will document the time of arrival and departure for all IRB members and notify the IRB Chair if a quorum is not present. Attendance is documented and maintained for each convened meeting.

It is generally expected that at least one unaffiliated member and at least one member who represents the general perspective of participants (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, individuals serving in this capacity must be present for at least 80% of the IRB meetings.

IRB members are considered present and participating at a duly convened IRB meeting when either physically present or participating through electronic means (e.g., teleconferencing or video conferencing) that permits them to listen to and speak during IRB deliberations and voting. When not physically present, the IRB member must have received all pertinent materials prior to the meeting and must be able to participate actively and equally in all discussions.

Comments of absent 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.

3.6.7 Meeting Procedures

The IRB Chair, or Vice-Chair in the event that the IRB Chair is absent, will call the meeting to order, once it has been determined that a quorum is met. In the event that both the Chair and Vice-Chair is absent, the board members present will vote to appoint a member to serve as Chair for the meeting. This vote will be documented in the meeting minutes. The Chair or Vice-Chair will remind IRB members to recuse themselves from the discussion and vote by leaving the room where there is a conflict. The IRB will review and discuss the IRB Minutes from the prior meeting and determine if there are any revisions/corrections to be made. If there are no changes to be made, the Minutes will be accepted as presented and considered final. If it is determined that revisions/corrections are necessary, the Minutes will be amended.

All members present at a convened meeting have full voting rights (whether in person or participating via tele/videoconference), except in the case of a conflict of interest (see below). In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting.

Voting

1. IRB members may not vote by proxy (i.e., members not present at the convened meeting or participating in the tele/videoconference call may not vote on an issue discussed during a convened meeting). However, members can provide written comments for IRB consideration.

2. Voting at a convened meeting takes place under the following conditions:

    - A majority of the members for a specific IRB must be present (or connected via speakerphone/video) for all reviews/actions voted on at a convened meeting;
    - A passing vote must consist of a majority of members present (or connected via speakerphone/video) voting in favor of the motion;
    - An individual who is not listed on the Office for Human Research Protections membership roster may not vote with the IRB;
    - Ex-officio members of the IRB may not participate in the vote;
    - Ad hoc and cultural consultants may not participate in the vote;
    - The non-scientist member must always be present for a vote;
    - A physician must be present to vote on FDA regulated research;

It is the responsibility of the IRB office staff to take minutes and record the proceedings of the meeting.

3.6.8 Guests

At the discretion of the IRB Chair, Principal Investigator for initial new submissions may be invited to the IRB meeting to answer questions about their proposed research. The Principal Investigator 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 HSPP, regularly attend IRB meetings. Ex-officio guests may fully participate in the IRB discussion and deliberations, but may not vote.

Other guests may be permitted to attend IRB meetings at the discretion of the IRB Chair and the Director of the IRB Office. Guests, other than ex-officio guests, may not speak unless requested by the IRB.

All guests, other than Principal Investigators, must sign a confidentiality agreement.

3.7 Criteria for IRB Approval of Research

In order for the IRB to approve human subjects research, either through expedited review or by the full IRB, 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 vulnerable populations, such as children, prisoners, pregnant women, 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 the Federal Regulations.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by the Federal Regulations.

(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, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

These criteria must be satisfied for each review (initial, continuing and modifications) for both expedited review and review by the convened IRB.

3.7.1 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:

- 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;
- disapprove 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 risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research;
2. determine whether the risks will be minimized to the extent possible;
3. identify the probable benefits to be derived from the research;
4. 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;
5. 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.

3.7.1.1 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 may draw on its own knowledge and disciplinary expertise, or the IRB may draw on the knowledge and disciplinary expertise of others, such as reviews by a funding agency, or departmental review. When scientific review is conducted by an individual or entity external to the IRB, documentation that the above questions were considered must be provided to the IRB for review and consideration.

3.7.2 Equitable Selection of Subjects

The IRB determines by viewing the application, protocol and other research project 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 vulnerable populations such as children, prisoners, pregnant women, mentally disabled persons, 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 IRB review and approval.

3.7.2.1 Recruitment of Subjects

The investigator will provide the IRB with all recruiting materials to be used in identifying participants including recruitment methods, advertisements, and payment arrangements.

3.7.3 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. In addition, the Committee 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.

3.7.4 Safety Monitoring

For all research that is more than minimal risk, the investigator must submit a safety monitoring plan. The initial plan submitted to the IRB should describe the procedures for safety monitoring, reporting of 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 that the safety monitoring plan makes adequate provision for monitoring the reactions of subjects and the collection of 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, low risk 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 problems to the IRB, sponsor and regulatory bodies as appropriate.
4. 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
- Procedures for reporting to the IRB

5. For a Data Safety Monitoring Board, the plan must include:
    - The name of the Data Safety Monitoring Board
    - Where appropriate, is an independent 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, IRBs 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.

3.7.5 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.

3.7.5.1 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 researchers about their subjects is not improperly divulged.

Private information - information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

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

3.7.5.2 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 in the situation. Investigators must have appropriate authorization to access the subjects or the subjects' information.

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

1. Methods used to identify and contact potential participants
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 participants and the nature of the requested information
5. Information that is obtained about individuals other than the "target participants," and whether such individuals meet the regulatory definition of "human participant" (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.

3.7.5.3 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 privacy and confidentiality of research subjects is protected. The IRB assesses whether there are adequate provisions to protect subject privacy and maintain confidentiality. The IRB does this through the evaluation of the methods used to obtain information:

a. About subjects,
b. About individuals who may be recruited to participate in studies
c. The use of personally identifiable records and
d. The methods to protect the confidentiality of research data.

The PI will provide the information regarding the privacy and 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 the privacy and confidentiality of research subjects 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 harms 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.

3.7.6 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 be put into place for vulnerable subjects, such as those without decision-making capacity.

3.8 Additional Considerations during IRB Review and Approval of Research

3.8.1 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,” “minor increase over minimal risk,” or “greater than minimal”. The meeting minutes will reflect the Committee’s determination regarding risk levels.

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

3.8.2.1 Review More Often Than Annually

Unless specifically waived by the IRB, research that meets any of the following criteria will require review more often than annually:

1. 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;
2. The involvement of especially vulnerable populations likely to be subject to coercion (e.g., terminally ill)
3. A history of serious or continuing non-compliance on the part of the PI.

The following factors will also be considered when determining which studies require review more frequently than on an annual basis:

1. The probability and magnitude of anticipated risks to subjects.
2. The likely medical condition of the proposed subjects.
3. The overall qualifications of the PI and other members of the research team.
4. The specific experience of the Responsible Investigator and other members of the research team in conducting similar research.
5. The nature and frequency of adverse events observed in similar research at this and other institutions.
6. The novelty of the research making unanticipated adverse events more likely.
7. Any other factors that the IRB deems relevant.

In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of subjects 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 year and that the number of subjects studied or enrolled determines the approval period only when that number of subjects is studied or enrolled in less than one year. If an approval period of less than one year is specified by the IRB the reason for more frequent review must be documented in the minutes.

3.8.3 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 occurred during the IRB-designated approval period. 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 and according to the following criteria:

1. Protocols where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources.

2. Protocols conducted by Principal Investigators who have previously failed to comply with federal regulations and/or the requirements or determinations of the IRB.
3. Protocols subject to internal audit.
4. Whenever else the IRB deems verification from outside sources is relevant.

The following factors will also be considered when determining which studies require independent verification:

1. The probability and magnitude of anticipated risks to subjects.
2. The likely medical condition of the proposed subjects.
3. The probable nature and frequency of changes that may ordinarily be expected in the type of research proposed.

In making determinations about independent verification, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period, or may retrospectively require such verification at the time of continuing review, review of amendments and/or unanticipated problems.

If any material changes have occurred without IRB review and approval, the IRB will decide the corrective action to be taken.

3.8.4 Consent Monitoring

In reviewing the adequacy of informed consent procedures for proposed research, the IRB may 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.

3.8.5 Investigator Conflicts of Interest

The research application asks protocol-specific questions regarding conflict of interest for the investigators and key personnel. As part of its review process, the IRB will make a determination as to whether a conflict of interest exists with regard to the research under review. If a conflict of interest exists, final IRB approval of a protocol cannot be given until an approved conflict management plan that adequately protects the human subjects in the protocol is in place.

3.8.6 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. 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.

3.8.7 Advertisements

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

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

This information should be submitted to the IRB with the initial application or as an amendment 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 investigational
5. Promising "free medical treatment" when the intent was only to say participants 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 of 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 IRB approval.

3.8.8 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 undue influence 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:

a) Substantiate that proposed payments are reasonable and commensurate with the expected contributions of the subject;

b) State the terms of the subject participation agreement and the amount of payment in the informed consent form; and

c). Substantiate that subject payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure on the veteran patient 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 participant 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).

3.8.9 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 HSPP and the IRB rely on the Institution Counsel for the interpretation and application of New Jersey State law and the laws of any other jurisdiction where research is conducted as they apply to the oversight of human subjects research by Rutgers IRBs.

3.9 Study Suspension, Termination and Investigator Hold

3.9.1 Suspension/Termination

IRB approval may be suspended or terminated if research is not being conducted in accordance with IRB or regulatory requirements or has been associated with unexpected problems or serious harm to subjects.

Suspension of IRB approval is a directive of the convened IRB or IRB Chair or the Director to temporarily stop some or all previously approved research activities short of permanently stopping all previously approved research activities. Suspension directives made by the IRB Chair or Director must be reported to a meeting of the convened IRB. Suspended protocols remain open and require continuing review.

Termination of IRB approval is 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. Terminations of protocols approved under expedited review must be made by the convened IRB.

The IRB shall notify the PI 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.

When study approval is suspended or terminated by the convened IRB or an authorized individual, in addition to stopping all research activities, the convened IRB or individual ordering the suspension or termination will notify any subjects currently participating that the study has been suspended or terminated. The convened IRB or individual ordering the suspension or termination will consider whether procedures for withdrawal of enrolled subjects are necessary to protect their rights and welfare of subjects, such as: transferring participants 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 participants 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.

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.)

Note: Suspension or termination of protocols approved by the IRB can also be issued by Rutgers officials acting outside of and unrelated to the HSPP (i.e., not necessarily related to protecting the rights and welfare of study participants). Such Rutgers' actions can be made by the Rutgers President, Vice President for Research, the Institutional Official, and School Deans. Such Rutgers' actions may be made for any reason in furtherance of the Institution's interest provided, however, that the aggrieved PI is entitled to all rights and procedures afforded to him/her under the Grievance Policy. The PI must report any suspension or termination of the conduct of research by Rutgers officials to the IRB. The IRB will then determine what further actions may be warranted.

3.9.2 Investigator Hold

An investigator may request an investigator hold on a protocol when the investigator wished to temporarily or permanently stop some or all approved research activities. An administrative hold is initiated by an investigator. Investigator holds are not suspensions or terminations.

3.9.2.1 Procedures

1. Investigators must notify the IRB in writing through a modification that:
    a. They are voluntarily placing a study on investigator hold
    b. A description of the research activities that will be stopped
    c. Proposed actions to be taken to protect current participants
    d. Actions that will be taken prior to IRB approval of proposed changes in order to eliminate apparent immediate harm
2. Upon receipt of written notification of the investigator the IRB office staff places the research on the agenda for review.
3. The IRB Chair and/or Director, in consultation with the investigators, determine whether any additional procedures need to be followed to protect the rights and welfare of current participants as described in "Protection of currently enrolled participants" below.

4. The IRB Chair and/or Director, in consultation with the investigators, determine how and when currently enrolled participants will be notified of the investigator hold.

3.9.3 Protection of Currently Enrolled Participants

Before an administrative or investigator hold, termination, or suspension, is put into effect the convened IRB or IRB designee considers whether any additional procedures need to be followed to protect the rights and welfare of current participants. Such procedures might include:

- Transferring participants to another investigator
- Making arrangements for clinical care outside the research
- Allowing continuation of some research activities under the supervision of an independent monitor
- Requiring or permitting follow-up of participants for safety reasons
- Requiring adverse events or outcomes to be reported to the IRB and the sponsor
- Notification of current participants
- Notification of former participants

3.10 Continuing Review

The IRB will conduct a continuing review of ongoing research at intervals that are appropriate to the level of risk for each research protocol, but not less than once per year. Continuing review must occur as long as the research remains active for long-term follow-up of participants, even when the research is permanently closed to the enrollment of new participants and all participants have completed all research-related interventions. Continuing review of research must occur even when the remaining research activities are limited to the analysis of private identifiable information.

3.10.1 Approval Period

Determination of the approval period and the need for additional supervision and/or participation is made by the IRB on a protocol-by-protocol basis. For example, for an investigator who is performing particularly risky research, or for an investigator who has recently had a protocol suspended by the IRB due to regulatory concerns, an on-site review by an IRB member or other designated individual might occur; or approval might be subject to an audit of study performance after a few months of enrollment, or after enrollment of the first several subjects.

For each initial or continuing approval the IRB will indicate an approval period with an approval expiration date specified. IRB approval is considered to have lapsed at midnight on the expiration date of the approval. For a study approved by the convened IRB, the approval period starts on the date that the IRB conducts its final review of the study; that is, the date that the convened IRB approved the research or the date the convened IRB deferred the research for non-substantive issues. For a study approved

under expedited review, the approval period begins on the date the IRB Chair or IRB member(s) designated by the Chair gives final approval to the protocol.

The approval date and approval expiration date are clearly noted on all IRB documents sent to the PI and must be strictly adhered to. Investigators should allow sufficient time for development and review of renewal submissions.

Review of a change in a protocol ordinarily does not alter the date by which continuing review must occur. This is because continuing review is review of the full protocol, not simply a change to it.

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

3.10.2 Continuing Review Process

To assist investigators, the IRB Office will send out renewal reminders in advance of the expiration date. However, it is the investigator's responsibility to ensure that the continuing review of ongoing research is approved prior to the expiration date. By federal regulation, no extension to that date can be granted.

Investigators must submit the following for continuing review:

1. a continuing review application noting any changes to the previously approved protocol;
2. the current consent document;
3. any newly proposed consent document; and
4. the current research protocol (if applicable)
5. Any research materials

In conducting continuing review of research not eligible for expedited review, all IRB members are provided and review all of the above material and the Primary Reviewer will review the complete protocol, including any modifications previously approved by the IRB. At the meeting, the Primary Reviewer Chair or designee, lead the IRB through the completion of the regulatory criteria for approval based upon the continuing review checklist. All study materials will be available to the IRB committee upon request.

In the case of expedited review, the IRB members may request the IRB office staff to provide them with any additional materials required for the review.

Review of currently approved or newly proposed consent documents must occur during the scheduled continuing review of research by the IRB, but informed consent documents should be reviewed whenever new information becomes available that would require modification of information in the informed consent document.

3.10.3 Expedited Review of Continuing Review

In conducting continuing review under expedited review, the reviewers receive all of the above material. The reviewer(s) complete the continuing review checklist to determine whether the research meets the criteria allowing continuing review using the expedited procedure, and if so, whether the research continues to meet the regulatory criteria for approval.

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, except in limited circumstances described by expedited review categories (8) and (9) at 63 FR 60364-60367 (see Expedited Review Categories). It is also possible that research activities that previously qualified for expedited review in accordance with 45 CFR 46.110, have changed or will change, such that expedited IRB review would no longer be permitted for continuing review.

3.10.4 Lapses 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. If the continuing review does not occur within the timeframe set by the IRB, all research activities must stop, including recruitment, 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 before the expiration date. It is generally recommended that investigators complete and submit a Continuing Review Application 4-6 weeks prior to the expiration of the study.

The IRB Office is responsible for immediately notifying the investigator of the expiration of approval and that all research activities must stop.

Enrollment of new subjects cannot occur and continuation of research interventions or interactions for already enrolled subjects should only continue when the IRB or IRB Chair finds that it is in the best interest of the individual subjects to do so.

Failure to submit continuing review information on time is non-compliance and will be handled according to the non-compliance policy.

Once approval has expired, IRB review and re-approval must occur prior to re-initiation of the research.

If a research protocol receives conditional approval at the time of the continuing review and the approval expires before the PI responds to the conditions, the PI may not enroll any new subjects or access records after the approval expiration date. Once the PI responds, the existing protocol will be reviewed for continuation. If the PI does not respond for an extended period, the IRB may vote to administratively close the study. Decisions of this kind must be made in a manner that ensures that closure will not harm

any participants previously enrolled who may require ongoing treatment as part of the research study.

3.11 Amendment of an Approved Protocol

Investigators may wish to modify or amend their approved applications. Investigators must seek IRB approval before making any changes in approved research - even though the changes are planned for the period for which IRB approval has already been given - unless the change is necessary to eliminate an immediate hazard to the subject (in which case the IRB must then be notified at once).

Modifications may be approved if they are within the scope of what the IRB originally authorized. For example, if a researcher 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.

Investigators must submit documentation to inform the IRB about the changes in the status of the study, including, but necessarily limited to:

- Completed a modification request form;
- Revised Investigator's protocol application or sponsor's protocol (if applicable)
- Revised approved consent/parental permission/assent documents (if applicable) or other documentation that would be provided to subjects when such information might relate to their willingness to continue to participate in the study
- Revised or additional recruitment materials
- Any other relevant documents provided by the investigator

IRB Office staff will determine whether the proposed changes may be approved through an expedited review process, if the changes are minor, or whether the modification warrants full board review. The Chair/designee using the expedited procedure has the ultimate responsibility to determine that the proposed changes may be approved through the expedited review procedure and, if not, must refer the protocol for full board review and approval.

3.11.1 Expedited review of Protocol Modifications

An 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 modification reviewer checklist 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 will also consider whether information about those modifications might relate to participants' willingness to continue to take part in the research and if so, whether to provide that information to participants.

3.11.2 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.

All IRB members are provided and review all documents provided by the investigator.

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

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

3.12 Closure of Protocols

The completion or termination of the study, whether premature or not, is a change in activity and must be reported to the IRB. 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 providing information that may be used by the IRB in the evaluation and approval of related studies.

Investigators may submit a final report to the IRB at any time.

3.13 Reporting IRB Actions

All IRB actions are communicated to the Principal Investigator (PI), and/or designated primary contact person for the protocol, in writing within approximately ten (10) working days via a template letter prepared by the IRB staff and signed by the IRB Chair or designee. For an approval, along with written notification of approval, a copy of the approved consent form containing the stamped approval with the dates of the approval and expiration on each sheet will be sent to the investigator. For a conditional approvals, the notification will include the modifications required for approval along with the basis for requiring those modifications. For a disapproval, termination or suspension, the notification will include the basis for making that decision.

All letters to investigators must be filed in the protocol files maintained by the IRB

The IRB reports its findings and actions to the institution in the form of its minutes, which are distributed by IRB staff to the Rutgers IO and are stored permanently and securely in the IRB Office.

3.14 Appeal of IRB Decisions

When an IRB protocol presented at a convened meeting is disapproved or deferred, 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 person or in writing. The IRB will carefully and fairly evaluate the investigator's response in reaching its final determination. There is no limit to the number of times a research project can be revised and re-submitted to the IRB for consideration.

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 determinations for approval remain under the purview of the IRB.

Since the IO is responsible for policies and procedures followed by the IRB, the IO may review IRB decisions to ensure that the decision-making process is appropriate. If the IO has concerns regarding the process that the IRB has followed in making a decision, he/she may request the IRB to reconsider the decision. However, the IO cannot overrule an IRB decision.

4 Documentation and Records

Rutgers prepares and maintains adequate documentation of the IRB's activities. All records are 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.

4.1 IRB Records

IRB records include, but are not limited to:

1. Written operating procedures.
2. IRB membership rosters,
3. Training records.
4. IRB correspondence
5. IRB 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
9. Documentation of convened IRB meetings minutes
10. Documentation of review by another institution's IRB when appropriate.
11. Documentation of cooperative review agreements, e.g. Memoranda of Understanding (MOUs).
12. Federal Wide Assurances.
13. Protocol deviations/violations submitted to the IRB
14. Quality assurance reviews.

4.2 IRB Study Files

The IRB maintains a separate IRB study file for each research application (protocol) that it receives for review. New protocol submissions are assigned a unique identification number when entered into the IRB tracking system.

Accurate records are maintained of all communications to and from the IRB. Copies are filed in the Principal Investigator's project file. Rutgers IRB maintains a separate file for each research protocol that includes, but is not limited to:

1. Protocol and all other documents submitted as part of a new protocol application.
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 participants, 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 IRB-approved Consent Form

5. IRB reviewer forms

6. Documentation of type of IRB review.

7. For expedited review, documentation of 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.

8. Documentation of all IRB review actions.

9. Notification of expiration of IRB approval to the PI and instructions for submitting relevant continuing review materials.

10. Notification of suspension of research.

11. Correspondence pertaining to appeals.

12. Copies of approval letters and forms that describe what Principal Investigator must have before initiating the study.

13. IRB correspondence to and from research investigators.

14. All other IRB correspondence related to the research.

15. For devices, documentation of determination by IRB of significant risk/non-significant risk and a report of prior investigations (if applicable).

16. Reports of unanticipated problems involving risk to subjects or others and adverse events.

17. Documentation of audits, investigations, reports of external site visits.

4.3 The IRB Minutes

Proceedings are prepared and available for review at a regularly scheduled IRB meeting date no more than three months later. Once approved by the members at a subsequent IRB meeting, the minutes must not be altered by anyone including a higher institutional authority.

A copy of IRB-approved minutes for each IRB meeting will be distributed to the IO.

Minutes of IRB meetings must contain sufficient detail to show:

1. Attendance
    a. Names of members present

b. Names of members or alternate members who are participating through videoconference or teleconference and documentation that those attending through videoconferencing or teleconferencing received all pertinent material prior to the meeting and were able to actively and equally participate in all discussions

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

d. Names of consultants present

e. Name of investigators present

f. Names of guests present

Note: The initial attendance list shall include those members present at the beginning of the meeting. The minutes will indicate, by name, those members who enter or leave the meeting. 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 IRB
6. Votes on these actions (Total Number Voting; Number voting for; Number voting against; Number abstaining; Number of those excused, Number of those recused)
7. Basis or justification for these actions including required changes in research
8. Summary of controverted issues and their resolution
9. Approval period for initial and continuing approved protocols, including identification of research that warrants review more often than annually and the basis for that determination
10. Risk level of initial and continuing approved protocols
11. Review of interim reports, e.g. unanticipated problems or safety reports; amendments; report of violation/deviations; serious or continuing non-compliance; suspensions/terminations, etc.
12. Review of Data and Safety Monitoring Board (DSMB) summary
13. Review of Plans for Data and Safety Monitoring

14. 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
15. Protocol-specific documentation that the research meets the required criteria [45 CFR 46.117(c)] when the requirements for documentation of consent are waived
16. When approving research that involves populations covered by Subparts B, C, or D of 45 CFR 46, the Minutes will document the IRB's justifications and findings regarding the determinations stated in the Subparts or the IRB's agreement with the findings and justifications as presented by the investigator on IRB forms.
17. Special protections warranted in for other groups of subjects who are likely to be vulnerable to coercion or undue influence, such as decisionally- impaired persons, or economically or educationally disadvantaged persons, regardless of source of support for the research.
18. The rationale for significant risk/non-significant risk device determinations.
19. Determinations of conflict of interest.
20. 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.
21. A list of research approved since the last meeting utilizing expedited review procedures.
22. An indication that, when an IRB member has a conflicting interest 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.
23. Key information provided by consultants will be documented in the minutes or in a report provided by the consultant

4.4 IRB Membership Roster

A membership list of IRB members will be maintained in the IRB office. The list will 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 Institution)
4. Status as scientist (physician-scientist, other scientist, or non-scientist).

5. Indications of experience, such as board certifications or licenses sufficient to describe each member's chief anticipated contributions to IRB deliberations.
6. Representative capacities of each IRB member; which IRB member is a prisoner representative (as required by Subpart C), and which IRB members are knowledgeable about or experienced in working with children, pregnant women, cognitively impaired individuals, and other vulnerable populations locally involved in research.
7. Role on the IRB (Chair, Vice Chair, etc.)
8. Voting status
9. For alternate members, the primary member or class of members for whom the member could substitute

The IRB office must keep the IRB membership list current. The Director of the IRB office must promptly report changes in IRB membership to the Office for Human Research Protections, Departments of Health and Human Services.

4.5 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 for satisfies the conditions of the cited exemption category as detailed in Section 3.6. The exempt determination is reported at a convened IRB meeting and documented in the minutes.

4.6 Documentation of Expedited Reviews

IRB records for initial and continuing review by the expedited procedure must include: the specific permissible category; that the activity described by the investigator satisfies all of the criteria for approval under expedited review; the approval period and any determinations required by the regulations including protocol-specific findings supporting those determinations.

4.7 Access to IRB Records

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

1. All IRB records are kept secure in filing cabinets, storage rooms, or on password-protected secure electronic server. Doors to the IRB Offices are closed and locked when the rooms are unattended.

2. Ordinarily, access to all IRB records is limited to the Director, IRB Chair, IRB members, IRB Administrator, IRB staff, authorized institutional, and officials of Federal and state regulatory agencies (OHRP, FDA). Research investigators are provided reasonable access to files related to their research. 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 IO, the Chief HSPP, and IRB Director.

3. Records are accessible for inspection and copying by authorized representatives of Federal regulatory agencies during regular business hours.

4. Records may not be removed from the IRB/HSPP Offices; however, the IRB staff will provide copies of records for authorized personnel if requested.

5. All other access to IRB study files is prohibited.

4.8 Record Retention

IRB Records pertaining to human subject research must be retained in compliance with all applicable federal, state, contractual, or institutional requirements (at a minimum of three years).

5 Obtaining Informed Consent from Research Subjects

No investigator conducting research under the auspices of the Institution 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 5.9 of these procedures, informed consent must be documented by the use of a written consent form approved by the . IRB will evaluate both the consent process and the procedures for documenting informed consent to ensure that adequate informed consent is obtained from participants.

The following procedures describe the requirements for obtaining consent from participants in research conducted under the auspices of Rutgers.

5.1 Definitions

Legally Authorized Representative A legally authorized representative is an individual or body authorized under applicable law to provide permission on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

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

5.2 Basic Requirements

The requirement to obtain the legally effective informed consent of individuals before involving them in Research is one of the central protections provided for by the Federal regulations and Rutgers. Investigators are required to obtain legally effective informed consent from a subject or the subject's Legally Authorized Representative. When informed consent is required, it must be sought prospectively, and properly documented.

The informed consent process involves three key features: (1) disclosing to the prospective human subject information needed to make an informed decision; (2) facilitating the understanding of what has been disclosed; and (3) promoting the voluntariness of the decision about whether or not to participate in the Research.

Informed consent is more than just a signature on a form. It is a process of information exchange to include reading and signing the informed consent document. The informed consent process is the critical communication link between the prospective Human Subject and an Investigator, beginning with the initial approach of an Investigator and continuing through the completion of the Research study. Investigators must have received the appropriate training and be knowledgeable about the study Protocol in order that they may answer questions to help provide understanding to the study participant or potential study potential study participant. The exchange of information between the Investigator and study participant can occur via one or more of the following modes of communication, among others; face to face contact, mail; telephone; internet, or fax.

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.

If someone other than the investigator conducts the interview and obtains consent from a potential subject, the investigator needs to delegate this responsibility, and the person so delegated must have received appropriate training 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.

In requesting approval to delegate consenting responsibilities, the PI must provide documentation the proposed delegated consenter training

Sample or draft consent documents may be developed by a Sponsor or cooperative study group. However, the IRB-of-record is the final authority on the content of the consent documents that is presented to the prospective study subjects.

5.3 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 the subject's legally authorized representative). In accordance with this policy, the IRB requires that informed consent conferences include a reliable translator when the prospective subject does not understand the language of the person who is obtaining consent.
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 Institution or Rutgers' employees or agents are released from liability for negligence, or appear to be so released.

7. The PI is responsible for insuring that each prospective subject is adequately informed about all aspects of the research and understands the information provided. It is recommended that this be documented in the research records.

5.4 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 an understanding:

1. that the activity is research, not standard treatment
2. of the risks and benefits of a study
3. of the alternatives that are available if s/he does not participate
4. that, if s/he chooses not to participate, this decision 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.

5.5 Basic Elements of Informed Consent

To be valid, the consent process must provide the following basic elements of information to potential subjects:

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;
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;

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 participant; 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.
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. For FDA-regulated studies, the possibility that the Food and Drug Administration may inspect the records needs to be included in the statement regarding subject confidentiality.
10. For clinical trials requiring registration at Clinicaltrials.gov the following statement must be included: " A description of this clinical trial will be available on 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 website 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. (For example: 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. (For example: 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. (For example: Include when it is anticipated that subjects may have additional costs.)
5. The consequences of a subject's decision to withdraw from the research. (For example: Include when withdrawal from the research is associated with adverse consequences.
6. Procedures for orderly termination of participation by the subject. (For example: 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. (For example: 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. (For example: Include when the research involves more than minimal risk.)

5.6 Documentation of Informed Consent

Except as provided in Section 5.9 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 and dated by the subject or the subject's legally authorized representative at the time of consent.
2. A copy of the signed and dated consent form must be given to the person signing the form.
3. The consent form may be either of the following:
    a. A written consent document that embodies the basic and required additional elements of informed consent. The consent form may be read to the subject or the subject's legally authorized representative, but the subject or representative must be given adequate opportunity to read it before it is signed; or
    b. A short form written consent document stating that the elements of informed consent have been presented orally to the subject or the subject's legally authorized representative.

5.6.1 Use of short form

When this method is used:

i. the oral presentation and the short form written document (see sample attached) should be in a language understandable to the subject; and
ii. there must be a witness to the oral presentation; and
iii. the IRB must approve a written summary of what is to be said to the subject; and
iv. the short form document is signed by the subject;
v. the witness must sign both the short form and a copy of the summary; and
vi. the person actually obtaining consent must sign a copy of the summary; and
vii. a copy of the summary must be given to the subject or representative, in addition to a copy of the short form.

When this procedure is used with subjects who do not speak English, (i) the oral presentation and the short form written document (see sample attached) should be in a language understandable to the subject; (ii) the

IRB-approved English language informed consent document may serve as the summary; and (iii) the witness should be fluent in both English and the language of the subject. When the person obtaining consent is assisted by a translator, the translator may serve as the witness.

The IRB must receive all foreign language versions of the short form document as a condition of approval. 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.

5.7 Special Consent Circumstances

5.7.1 Non-English Speaking Subjects

1. **Expected enrollment of non-English speaking subjects**: In some protocols, the PI expects non-English speaking subjects to enroll because, for example, the protocol is studying a disease or condition that is likely to attract them or the PI is actively recruiting them. When the study subject population includes non-English speaking people or the PI and/or the IRB anticipates that consent discussions will be conducted in a language other than English, the IRB shall require a translated consent document to be prepared. In order to assure itself that the translation is accurate, the IRB may choose to require a certified translation, to have an independent back translation or to have a review of the consent document by an IRB member or other person who is fluent in that language. When non-English speaking subjects enroll, they and the witness sign the translated document. The subjects are given a copy of the signed translated consent document.
2. **Unexpected enrollment of a non-English speaking subject:** If a non-English speaking subject is unexpectedly eligible for protocol enrollment, there may not be an existing IRB-approved written translation of the consent document. Investigators should carefully consider the ethical and legal ramifications of enrolling subjects when a language barrier exists. If the subject does not clearly understand the information presented at the signing of the consent document or in subsequent discussions, his/her consent may not be informed, and therefore, not effective.

   If a PI decides to enroll a subject into a protocol for which there is not an existing IRB-approved informed consent document in the prospective subject's language, the PI must receive IRB approval to follow the procedures for a “short form” written consent.
3. **Use of interpreters in the consent process:** Unless the person obtaining consent is fluent in the prospective subject’s language, an interpreter will be necessary to deliver information in the IRB-approved script and to facilitate the consent conversation. Preferably someone who is independent of the subject (i.e., not a family member) should assist in presenting information and obtaining

consent. Whenever possible, interpreters should be provided copies of the short form and the IRB-approved consent script well before (24 to 48 hours if possible) the consent conversation with the subject. If the interpreter also serves as the witness, she/he may sign the short form consent document and script as the witness and should note “Interpreter” under the signature line. The person obtaining consent must document that the “short form” process was used in the progress notes of the subject's medical record, including the name of the interpreter.

5.7.2 Braille consent

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 verbal consent will be obtained, witnessed and documented as described below.

5.7.3 Consenting 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 prospective subjects must use an Rutgers-certified 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 5.6.1.

5.7.4 Oral Consent

When subjects are unable to read a written consent form (such as blind or illiterate subjects), the IRB may approve an oral 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.

For research that is no more than minimal risk, documentation of consent may be waived according to the criteria in Section 5.10

For more than minimal risk research, 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 verbal consent. 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 verbal consent. The consent process will be documented in the research and, if applicable, 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 should be provided to the subject on audio or video tape.

5.8 Consent Monitoring

In reviewing the adequacy of informed consent procedures for proposed research, the IRB may 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, ensure that the approved consent process is being followed, or ensure that subjects are truly giving informed consent.

Such monitoring may be particularly warranted for:

1. High risk studies
2. Studies that involve particularly complicated procedures or interventions
3. Studies involving highly vulnerable populations (e.g., ICU patients, children)
4. Studies involving study staff with minimal experience in administering consent to potential study participants, or
5. Other situations when the IRB has concerns that consent process is not being conducted appropriately.

Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with a particular investigator or a research project.

If the IRB determines that consent monitoring is required, the IRB Committee will develop a monitoring plan.. The consent monitoring may be conducted by IRB staff, IRB members or another party, either affiliated or not with the institution. The PI will be notified of the IRB's determination and the reasons for the determination. Arrangements will be made with the PI for the monitoring of the consent process for a specified number of subjects. When observing the consent process, the monitor will determine:

- Whether the informed consent process was appropriately completed and documented,
- Whether the participant had sufficient time to consider study participation,
- Whether the consent process involved coercion or undue influence,
- Whether the information was accurate and conveyed in understandable language, and
- Whether the subject appeared to understand the information and gave their voluntary consent.

Following the monitoring, a report of the findings will be submitted to the IRB, which will determine the appropriate action to be taken.

5.9 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 between research subjects to FDA regulations and that not subject to FDA regulations. Under applicable FDA law and regulations, data collected on human subjects enrolled in an FDA-regulated clinical trial up to the time of subject withdrawal must remain in the trial database in order for the study to be scientifically valid. For research not subject to FDA regulations, investigators, in consultation with the funding agency, can choose to 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.

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: (1) obtaining data about the subject through interaction with the subject (e.g., through follow-up interviews, physical exams, blood tests, or radiographic imaging); or (2) 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. 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

5.10 Waiver of Informed Consent

An IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth above; or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

(a) The research involves no more than minimal tangible or intangible risk to the subjects;

(b) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(c) The research could not practicably be carried out without the waiver or alteration; and

(d) Whenever appropriate, the subjects must be provided with additional pertinent information after participation.

In addition, an IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent; or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

(a) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:

1. Public benefit or service programs

2. Procedures for obtaining benefits or services under those programs

3. Possible changes in or alternatives to those programs or procedures; or

4. Possible changes in methods or levels of payment for benefits or services under those programs.

(b) The research could not practicably be carried out without the waiver or alteration.

FDA regulations do not provide for waivers of informed consent except in emergency situations.

5.11 Waiver of Documentation of Informed Consent

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either that the:

1. Only record linking the subject and the research would be the consent document and the principle risk would be potential harm resulting from a breach of confidentiality; or
   Note 1: Subjects 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 researchers.)
   Note 2: In order to waive written documentation of consent where the only record linking the participant and the research would be the consent document, the IRB has to determine that the research was not FDA-regulated.
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. Procedures such as non-sensitive surveys, questionnaires and interviews generally do not require written consent when conducted by non-researchers (e.g., marketing surveys, telemarketing) .

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, and the IRB will consider whether to require the investigator to provide subjects with a written statement regarding the research.

5.12 Waiver of Informed Consent for Planned Emergency Research

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.

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 (participants) who are in need of emergency medical intervention

cannot provide legally effective informed consent and their legally authorized representatives (LARs) are unable to give informed consent as well.

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).*

5.12.1 Definition

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

5.12.2 Procedures

The IRB may approve the planned emergency research without requiring informed consent of all research subjects prior to initiating the research intervention if the IRB finds and documents that the following conditions 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:

> (i) The subjects will not be able to give their informed consent as a result of their medical condition;
>
> (ii) The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and
>
> (iii) 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:

> (i) Subjects are facing a life-threatening situation that necessitates intervention;
>
> (ii) 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
>
> (iii) 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 Sections 46.116 and 46.117 of 45 CFR 46 and Sections 20, 25 and 27 of 21 CFR 50. 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)(v) of this section.

(7) Additional protections of the rights and welfare of the subjects will be provided, including, at least:

(i) 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;

(ii) 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;

(iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;

(iv) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and

(v) 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.

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.

5.12.2.1 FDA-regulated Research

1) Studies 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 studies as protocols that may include subjects who are unable to consent. The submission of those studies 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 312.30 or 812.35 of this chapter.

2) If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under paragraph (a) of 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 IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

3) The IRB determinations and documentation required in Section 5.11.2 and paragraph 2 above are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with 56.115(b) of this chapter.

5.12.2.2 Research Not Subject to FDA Regulations

1) The IRB responsible for the review, approval, and continuing review of the research has approved both the research and a waiver of informed consent and has (i) found and documented that the research *is not subject* to regulations codified by the FDA at 21

CFR Part 50, and (ii) found and documented and reported to the OHRP that the conditions required Section 5.11.2 have been met relative to the research

2) For the purposes of this waiver "family member" means any one of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship.

5.12.3 Community Consultation

Community Consultation assures that the concerns of the community in which emergency research will take place are addressed during the research review process. The plan for community consultation must be approved by the IRB Chair or designee and the Institute Official. The PI is responsible for obtaining community consultation, incorporating community concerns into the written protocol and providing information on community concerns to the IRB for their review. Community consultation may include of any of the following activities:

- Surveys or questionnaires,
- Focus groups or
- Community meetings.

If community meetings are held, the meetings must include the Principal Investigator, a representative from the institution, and where required by the IRB, a member of the IRB.

Populations surveyed for the Community Consultation should include those in the community in from which the subjects will be drawn, especially those affected by the disease or condition under study.

Information provide for community consultant consideration includes the investigational plan, its risks and its expected benefits to the individual and to the community.

6 Vulnerable Subjects in Research

When some or all of the participants in a research conducted under the auspices of Rutgers 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 participants. 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 participants in research under the auspices of Rutgers.

6.1 Definitions

Children 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. According to New Jersey State Law, minors are persons under the age of eighteen. The general rule is that a person may consent for his or her own medical care at the age of eighteen. Therefore, Rutgers' IRB generally defines children as persons under eighteen years of age.

NOTE: For research conducted in jurisdictions other than [New Jersey the research must comply with the laws regarding the legal age of consent in all relevant jurisdictions.

Guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. In New Jersey a "Guardian" of a minor means the duty and authority to act in the best interests of the minor, subject to residual parental rights and responsibilities, to make important decisions in matters having a permanent effect on the life and development of the minor and to be concerned with his or her general welfare.

NOTE: For research conducted in jurisdictions other than New Jersey the research must comply with the laws regarding guardianship in all relevant jurisdictions.

Fetus means the product of conception from implantation until delivery.

Dead fetus means a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

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

Neonate means a newborn.

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

Nonviable neonate means a neonate after delivery that, although living, is not viable.

Pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs

of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

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

Surrogate Consent is consent obtained from a legally authorized representative on behalf of a participant determined to lack decision-making capacity.

6.2 Involvement of Vulnerable Populations

When some or all of the participants 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 participants. Some of the vulnerable populations that might be involved in research include children, pregnant women, fetuses, neonates, prisoners, or adults who lack the ability to consent, students, employees, or homeless persons.

If the IRB reviews research that involves categories of participants 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 participants. 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.

45 CFR 46 has additional subparts designed to provide extra protections for vulnerable populations which also have additional requirements for IRBs.

> 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

DHHS-funded research that involves any of these populations must comply with the requirements of the relevant subparts. Research funded by other federal agencies may or may not be covered by the subparts.

Under Rutgers' FWA the subparts only apply to DHHS-funded research and research funded by another federal agency that requires compliance with the subparts (FDA regulations include Subpart D, which applies to all FDA-regulated research). The following policies and procedures, which are based on the subparts, apply to all research regardless of funding. The individual sections describe how the subparts apply to DHHS-funded research.

6.3 Responsibilities

1. The PI is responsible for identifying the potential for enrolling vulnerable subjects in the research proposal. The PI is responsible for identifying patients who are at risk for impaired decisional capacity as a consequence of psychiatric illness, and who are being asked to participate in a research study with greater than minimal risk.
2. The IRB shall include representation, either as members or ad hoc consultants, individual(s) interested in or who have experience with the vulnerable populations involved in a research proposal.
3. The IRB reviews the PI's justifications for including vulnerable populations in the research to assess appropriateness of the research proposal.
4. The IRB must ensure that additional safeguards have been included in each study to protect the rights and welfare of vulnerable subjects as needed at the time of initial review of the research proposal.
5. Information reviewed as part of the continuing review process should include the number of participants considered as members of specific vulnerable populations.
6. For studies that do not have or are not required to have a Data and Safety Monitoring Board (DSMB) or a Data Monitoring Committee and have entered vulnerable subjects, the IRB needs to carefully review the safety monitoring plan.
7. The IRB should be knowledgeable about and experienced in working with populations who are vulnerable to coercion and undue influence. If the IRB requires additional qualification or expertise to review a protocol, it should obtain consultation.

6.4 Procedures

Initial Review of Research Proposal:

1. The PI should identify the potential to enroll vulnerable subjects 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 participants.
4. The IRB evaluates the research to determine the need for additional protections and consider the use of a data and safety monitoring board or data monitoring committee as appropriate.

5. The PI should provide appropriate safeguards to protect the subject's rights and welfare, which may include the addition of an independent monitor. The independent monitor is a qualified individual not involved in the research study who will determine the subject's capacity to provide voluntary informed consent.
6. Examples of studies that warrant independent monitoring include those involving schizophrenic patients who will be exposed to placebo, and/or drug washout, and/or treatment with agents that are not approved by the Food and Drug Administration (FDA). Populations requiring independent monitoring would include individuals with schizophrenia, other psychotic disorders or conditions characterized by lack of reality testing (i.e., psychosis). Populations not usually requiring independent monitoring would include those with substance use disorders.
7. The IRB assess the adequacy of additional protections for vulnerable populations provided by the PI.

6.5 Research Involving Pregnant Women, Human Fetuses and Neonates

Since, according to Rutgers' FWA, Subpart B of 45 CFR 46 applies only to DHHS-funded research, the funding-source specific requirements are noted in the appropriate sections.

6.5.1 Research Involving Pregnant Women or Fetuses

6.5.1.1 Research Not Funded by DHHS

For research not funded by DHHS, 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 no more than minimal.

Pregnant women or fetuses may be involved in research not funded by DHHS involving more than minimal risk to fetuses 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.

6.5.1.2 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 10.1.3;
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.

6.5.2 Research involving 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.
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 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.
6. 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 IRB Review Process and Research Involving Children.

6.5.3 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.

6.5.4 Research Not Otherwise Approvable

6.5.4.1 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 6.2.2, as applicable; or
2. The following:

1. 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;
2. The research will be conducted in accord with sound ethical principles; and
3. Informed consent will be obtained in accord with the provisions for informed consent and other applicable sections of this manual.

6.5.4.2 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.

6.6 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 make prisoners ripe for exploitation.

The concern Subpart C and this policy based on Subpart C attempt 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.

6.6.1 Applicability

This policy applies to all biomedical and behavioral research conducted under the auspices of Rutgers involving prisoners as subjects. Even though the Rutgers 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 Jersey Department of Corrections and any other applicable State or local law. [45 CFR 46.301]

6.6.2 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.

6.6.3 Composition of the IRB

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 IRB, only one IRB need satisfy this requirement.
- The prisoner representative must be a voting member of the IRB. The prisoner representative may be listed as an alternative member who becomes a voting member when needed.

6.6.4 Review of Research Involving Prisoners

1. The prisoner representative must review research involving prisoners, focusing on the requirements in Subpart C.
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.

1. 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.
2. 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

1. 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.
2. 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.

6.6.5 Incarceration of Enrolled Subjects

If a participant 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 participant meets the definition of a prisoner.
2. Terminate enrollment or review the research study under Subpart C if it feasible for the participant to remain in the study.

3. Before terminating the enrollment of the incarcerated participant the IRB should consider the risks associated with terminating participation in the study. If the participant cannot be terminated for health or safety reasons, one of two options are available:

1. Keep the participant enrolled in the study and review the research under Subpart C. If some the requirements of Subpart C cannot be met, but it is in the best interests of the participant to remain in the study, keep the participant enrolled and inform OHRP of the decision along with the justification.
2. Remove the participant from the study and keep the participant on the study intervention under an alternate mechanism such as compassionate use, off label use, etc.

4. If a participant is incarcerated temporarily while enrolled in a study:

5. If the temporary incarceration has no effect on the study, keep the participant enrolled.
6. If the temporary incarceration has an effect on the study, handle according to the above guidance.

6.6.6 Additional Duties of the IRB

In addition to all other responsibilities prescribed for IRB in Rutgers 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:

- the research falls into one of the following permitted categories [45 CFR 46.306]:
  - 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;
  - 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;
  - 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);
  - research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject.
- 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;

- the risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
- 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;
- the information is presented in language which is understandable to the subject population;
- 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
- 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.

6.6.7 Certification to HHS

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 Rutgers 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 Rutgers on behalf of the Secretary under 45 CFR 46.306(a)(2).

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.

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

6.6.8 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:

7. In which the sole purposes are

1. To describe the prevalence or incidence of a disease by identifying all cases, or
2. To study potential risk factor associations for a disease, and

8. Where the IRB has approved the research and fulfilled its duties under 45 CFR 46.305(a)(2)–(7) and determined and documented that

1. The research presents no more than minimal risk and no more than inconvenience to the prisoner-subjects, and
2. Prisoners are not a particular focus of the research.

9. The specific type of epidemiological research subject to the waiver involves no more than minimal risk and no more than inconvenience to the human subject participants. 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).
10. 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.
11. 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.

6.7 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.

6.7.1 Allowable Categories

Research on children must be reviewed and categorized by the IRB into one of the following groups:

1. 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

2. 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 6.7.2.
3. 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 6.7.2.
4. 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 6.7.2.

6.7.2 Parental Permission and Assent

6.7.2.1 Parental Permission

The IRB must determine that adequate provisions have been made for soliciting the permission of each child's parent or guardian.

Parents or guardians must be provided with the basic elements of consent and any additional elements the IRB deems necessary, as described in Section 5.5.

The IRB may find that the permission of one parent is sufficient for research to be conducted under Categories 1 & 2 above. The IRB's determination of whether consent must be obtained from one or both parents will be documented in the consent checklist 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 Categories 3 & 4 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.

For research not covered by the FDA regulation, the IRB may waive the requirement for obtaining consent from a parent or legal guardian if:

- The research meets the provisions for waiver in Section 5.8 or
- 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 (for example, 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.

Parental permission may not be waived for research covered by the FDA regulations.

Permission from parents or legal guardians must be documented in accordance with and to the extent required by Section 5.6 and 5.9.

6.7.2.2 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, the IRB is charged with taking into account the ages, maturity, and psychological state of the children involved. The IRB has the discretion to judge children's capacity to assent for all of the children to be involved in a proposed research activity, or on an individual basis.

The IRB should take into account the nature of the proposed research activity and the ages, maturity, and psychological state of the children involved when reviewing the proposed assent procedure and the form and content of the information conveyed to the prospective subjects. For research activities involving adolescents whose capacity to understand resembles that of adults, the assent procedure should likewise include information similar to what would be provided for informed consent by adults or for parental permission. For children whose age and maturity level limits their ability to fully comprehend the nature of the research activity but who are still capable of being consulted about participation in research, it may be appropriate to focus on conveying an accurate picture of what the actual experience of participation in research is likely to be (for example, what the experience will be, how long it will take, whether it might involve any pain or discomfort). The assent procedure should reflect a reasonable effort to enable the child to understand, to the degree they are capable, what their participation in research would involve.

The IRB presumes that children ages 7 and older should be given an opportunity to provide assent. Generally, oral assent through the use of a script should be obtained from children 7 - 11 years of age. Written assent using a written document for the children to sign may be sought for older children.

At times there may be inconsistency between parent permission and child assent. Usually a "no" from the child overrides a "yes" from a parent, but a child typically cannot decide to be in research over the objections of a parent. Obviously, there are individual exceptions to these guidelines (such as when the use of an experimental treatment for a life threatening disease is being considered). The general idea, however, is that children should not be forced to be research subjects, even when their parents consent to it.

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 not 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.

The Assent Form

When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

Researchers 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. ask for questions.

For younger children, the document should be limited to one page if possible. Illustrations might be helpful, and larger type makes a form easier for young children to read. Studies involving older children or adolescents should include more information and may use more complex language.

6.7.2.3 Children who are Wards

Children who are wards of the State or any other agency, institution, or entity can be included 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, **only if such research** is:

3. related to their status as wards; or
4. 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, 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 Institution.

6.8 Persons with Impaired Decision Making Capacity

The requirements in this section apply to all research involving persons with mental disabilities or persons with impaired decision-making capacity regardless of funding source. All procedures involving surrogate consent must be in compliance with the NJ “Access to Medical Research Act.”

6.8.1 Determination of Decision-Making Capacity

The decision-making capacity of a potential research subject should be evaluated when there are reasons to believe that the subject may not be capable of making voluntary and informed decisions about research participation.

The investigator and research staff must have adequate procedures in place for assessing and ensuring subjects' capacity, understanding, and informed consent or assent. The IRB will evaluate whether the proposed plan to assess capacity to consent is adequate.

For research protocols that involve subjects with mental disorders that may affect decision-making capacity, the IRB may determine that capacity assessments are necessary, unless the investigator can justify why such assessments would be unnecessary for a particular group.

For research that poses greater than minimal risk, the IRB may require investigators to use independent and qualified professionals to assess whether potential subjects have the capacity to give voluntary, informed consent. Even in research involving only minimal risk, the IRB may require that the study include a capacity assessment if there are reasons to believe that potential subjects' capacity may be impaired. It is not necessary to require a formal capacity assessment by an independent professional for all potential research subjects with mental disorders.

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.

Although incompetent to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may subjects be forced or coerced to participate.

In the event research participants become incompetent or impaired in decision making capacity after enrollment, the PI is responsible for notifying the IRB and Research office.

The PI is responsible for developing a monitoring plan which follows the guidelines outlines above for incompetent and impaired decision making research participants.

6.8.2 Surrogate Consent

In the state of New Jersey, research involving the use of surrogate consent must be in compliance with the New Jersey "Access to Medical Research Act." In order to ensure this compliance, Rutgers University requires that the following procedures be followed when obtaining surrogate consent:

I. Investigator Responsibilities:

A. IRB Approval

The investigator must apply to the IRB for use of surrogate consent that is specific to the particular study being reviewed. Upon approval by the IRB, the investigator shall apply the use of surrogate consent on a case-by-case basis within that protocol.

1. New Studies: An investigator must indicate in the IRB Application for Initial Review that the protocol will utilize a surrogate consent process and must provide a complete description of the Investigator's plan to obtain the surrogate's consent as by completing Appendix H, the Surrogate Consent Process Addendum. An investigator must receive IRB approval prior to implementation of surrogate consent procedures for a specific study.

2. Ongoing Studies: If an investigator decides to utilize the surrogate consent process for a Study that has already received IRB approval, a Request for Modification Form must be submitted to the IRB. An investigator must receive IRB approval for this modification prior to implementation of surrogate consent procedures for a specific study.

B. Determination of Incapacity

1. Whenever possible, investigators will attempt to obtain informed consent directly form the subject.

2. If the subject has an advance directive for healthcare and has indicated that s/he does not wish to participate in a research study, the potential subject must not be included in the study.

3. A determination that the subject is unable to consent, as well as the extent of the incapacity and the likelihood that s/he will regain decision-making capacity, must be made by an attending physician with no connection to the study. This determination must be documented by the attending physician making the determination.

For purposes of this section, inability to consent shall mean that a subject is unable to voluntarily reason, understand, and appreciate the nature and consequence of proposed health research interventions, including the subject's diagnosis and prognosis, the burdens, benefits, and risks of, and alternatives to, any such research, and to reach an informed decision.

4. The investigator must assure that the determination of incapacity is promptly given to the subject and to at least one person at the highest category reasonably available on the list of surrogates in subsection C3 below.

C. Identification of Surrogate

1. If the investigator believes that a subject lacks decision-making capacity, the investigator shall inform the subject about the study and of the investigator's intention to seek a surrogate to provide consent.
2. **If the subject expresses resistance or dissent to participation or to the use of a surrogate for consent, the investigator must exclude the subject from the study.**

3. Surrogate informed consent may be obtained from an authorized representative with reasonable knowledge of the subject, who shall include any of the following persons, in the following descending order or priority:

i. the guardian of the subject with the authority to make health care decisions;
ii. the health care representative pursuant to an advance directive for health care;
iii. the spouse or civil union partner;
iv. a domestic partner;
v. an adult son or daughter;
vi. a custodial parent;
vii. an adult brother or sister;
viii. an adult grandchild; **or**
ix. an available adult relative with the closest degree of kinship.

4. The investigator must make a good faith effort to contact the individual at the highest level of priority. These efforts should be documented. Potential surrogates must be advised that if a higher-ranking surrogate is identified at any time, the investigator whenever feasible will defer to the higher-ranking surrogates' decision regarding the subject's participation in the research.

5. The investigator must assure that if one of two or more available persons in the same order or priority expresses opposition to the participation of the subject in the study, the investigator must exclude the subject from the study.

6. The investigator must assure that when two or more available persons are in different orders of priority, refusal to consent by a potential surrogate who is of a higher priority controls and cannot be superseded by the consent of a person who is of a lower priority.

D. Obtaining Surrogate Consent

1. Surrogates for a potential research subject may not receive financial compensation for providing consent.

2. Surrogates must review, sign and date the Surrogate Self-Certification Form and the IRB- approved Surrogate Consent Form prior to providing surrogate consent for study participation.

3. The investigator or designee must orally review each element included in the Surrogate Consent Form with the surrogate. This oral review must be in non-technical terms and in a language in which the surrogate is fluent.

4. The investigator must assure that a copy of the Surrogate Consent Form is given to the surrogate.

E. If a Subject Regains Cognitive Ability

In the event that a subject regains the cognitive ability to consent to participation in the study, the Investigator must assure that the subject is promptly consented using standard consent procedures.

F. Documentation

1. The principal investigator must use a study specific, IRB-approved Surrogate Consent Form and ensure that:

    a. the principal investigator or his/her designee signs and dates the Surrogate Consent Form
    b. the subject's surrogate signs and dates the Surrogate Consent Form
    c. The Surrogate Consent Form is signed and dates by a witness who is not the subject, the subject's guardian, surrogate, or member of the research team, and who can attest that the requirements for informed consent to the study have been satisfied.

2. In all cases involving the use of a surrogate, the principal investigator, or his/her IRB-approved designee obtaining surrogate consent shall file a completed Surrogate Consent Form in both the medical and research records.

3. The determination of a subject's incapacity to consent to study participation by the physician making the determination must be documented and retained

in both the medical and research records. This documentation must be retained as part of the permanent source documents for the IRB-approved study.

II. IRB Responsibilities:

A. In order to approve the use of a surrogate in a study, the IRB must make a determination and document that the research relates to the cognitive impairment, lack of capacity, or serious physical or behavioral conditions and life threatening diseases of the research subjects **and** either:

1. offers the prospect of direct benefit to the subject, provided that the IRB has determined that the risk is justified by the anticipated benefits and that the relation of the anticipated benefit to the risk is at least as favorable to the subject as that presented by available alternative approaches. If a currently recognized treatment exists, the subject, guardian, or surrogate shall be presented with the choice of the recognized treatment and the research protocol,

or

2. does not offer the prospect of direct benefit to the subject, provided that the IRB has determined that it: (1) is likely to yield generalizable knowledge about the subject's disorder or condition; (2) by its very nature cannot be conducted without the participation of decisionally incapacitated persons; and (3) involves no more than a minor increase over minimal risk. "Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine psychological exams or tests.

B. The IRB must ensure that all of the following elements are specified in the approved Surrogate Consent Form in nontechnical terms and in a language in which the subject or the subject's guardian or authorized representative is fluent.

1. an explanation of the procedures to be followed in the study and any drugs or devices to be utilized, including:

a) the purposes of the procedures, drugs, or devices;

b) the use of placebo controls, when applicable;

c) the process by which persons will be assigned to control groups.

2. an explanation of any potential direct benefits to the subject. If no such direct benefits are reasonably expected, that fact should be made clear.

3. a description of any attendant discomfort and reasonably foreseeable risks to the subject.

4. a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

5. an estimate of the expected duration of the study.

6. the name, institutional affiliation, and address of the person or persons actually performing and primarily responsible for the conduct of the study;

7. an offer to answer any inquiries concerning the study or the procedures involved; and

    a) who to contact for answers to pertinent questions about the study
    b) whom to contact in the event of a study-related injury; and
    c) contact information for the institutional review board; and
    d) the name, address, and phone number of an impartial third party, not associated with the research to whom the subject/surrogate may address complaints.

8. instruction to the subject or surrogate that he/she is free to withdraw consent and discontinue participation in the study at any time, without prejudicing the subject's medical treatment outside the study;

9. a statement regarding the Investigator's plan to safely remove a subject from the study and any consequences of abruptly ending participation in the study;

10. the name of the sponsor or funding source, if any, or manufacturer if the study involves a drug or device, and the organization, if any, responsible for the general direction of the study; and

11. the material financial stake or interest, if any, that the investigator or research institution has in the study. (For purposes of this section, "material" means $10,000 or more in securities or other assets valued at the date of disclosure, or relevant cumulative salary or other income.)

C. The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

    1. The research involves no more than minimal risk to the subjects;

2. The waiver or alternation will not adversely affect the rights and welfare of the subjects

3. The research could not practicably be carried out without the waiver or alteration; and

4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

7 FDA-Regulated Research

FDA regulations apply to any research that involves a *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, as well as, where appropriate, 45 CFR 46.

Use of investigational drugs must be conducted according to FDA IND regulations, 21 CFR Part 312, and other applicable FDA regulations. Use of an investigational device in a clinical trial to obtain safety and effectiveness data 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 conducted under the auspices of Rutgers.

7.1 Definitions

Investigational Drug. An investigational drug for clinical research use is one for which the PI or a sponsor has filed an IND application (21 CFR Part 312) or an approved drug that is being studied for an unapproved or approved use in a controlled, randomized, or blinded clinical trial.

Investigational Device. A medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. As further stated, a device is any healthcare product that does not achieve its primary intended purpose by chemical action or by being metabolized.

IND. IND means an investigational new drug application in accordance with 21 CFR Part 312.

IDE. IDE means an investigational device exemption in accordance with 21 CFR 812.

Emergency Use. Emergency use is defined as the use of an investigational drug or biological product with 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.

Significant Risk (SR). Significant risk 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; 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.

Non-Significant Risk (NSR). A non-significant risk device is an investigational device other than a significant risk device.

Humanitarian Use Device (HUD). Humanitarian Use Device is a device intended to benefit patients by treating or diagnosing a disease that affects fewer than 4,000 individuals in the United States per year.

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 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. [21 CFR §56.104(d)]

7.3 Investigational Drugs and Devices in Research

7.3.1 IND/IDE Requirements

The PI must indicate on the IRB application whether the research involves investigational drugs or devices. If so, the PI must indicate if there is an IND/IDE for the research and provide documented assurance from the sponsor that the manufacture and formulation of investigational or unlicensed test articles conform to federal regulations. Documentation of the IND/IDE could be a:

1. Industry sponsored protocol with IND/IDE.
2. Letter from FDA.
3. Letter from industry sponsor.
4. Other document and/or communication verifying the IND/IDE.

For investigational devices, NSR device studies follow abbreviated IDE requirements and do not have to have an IDE application approved by the FDA (21 CFR 812.2(b)). If a sponsor has identified a study as NSR, then the investigator must provide an explanation of the determination. If the FDA has determined that the study is NSR, documentation of that determination must be provided.

If the research involves drugs or devices and there is no IND/IDE, the PI must provide a rationale why it is not required.

The IRB will review the application and determine:

1. Whether there is an IND/IDE and if so, whether there is appropriate supporting documentation.
2. If the research involves drugs or devices with no IND/IDE, and whether the research meets the criteria below.

7.3.1.1 IND Exemption

For drugs, an IND is not necessary if the research falls in one of the following categories:

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 in support of a new indication for use or to support any other significant change in the labeling for the drug
    b. 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 or dosage level, use in a 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 concerning the promotion and sale of drugs [21 CFR 312.7]
    f. The research does not intend to invoke FDA regulations for planned emergency research [21 CFR 50.24].
2. The research only involves one or more of the following: (a) Blood grouping serum, (b) Reagent red blood cells or (c) Anti-human globulin;
3. For clinical investigations involving an in vitro diagnostic biological product, 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
4. A clinical investigation involving use of a placebo is exempt from the requirements of this part if the investigation does not otherwise require submission of an IND.

7.3.1.2 Exempted IDE Investigation

For 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;

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.

7.3.2 Responsibilities

7.3.2.1 PI

1. The PI is responsible for ensuring that the research is conducted according to all regulatory guidelines and Rutgers' policies and procedures
2. The PI must obtain approval from the IRB before initiating any research activities.
3. The PI proposing the drug/device research will be required to provide a plan – to be evaluated by the IRB - that includes storage, security, and dispensing of the drug/biologics/device.
    a. The PI is responsible for the investigational drug/device accountability that includes storage, security, dispensing, administration, return, disposition, and records of accountability.
    b. The PI will indicate who maintains responsibility for drugs/biologics accountability .

c. 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 and the disposition of remaining devices at the conclusion of the investigation.

4. The PI shall report all unanticipated problems involving risk to subjects or others to the IRB according to the procedures outlined in Section 8.

5. For research involving investigational new drugs:

    a. The PI will report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug (21 CFR 312 (b)) according to the procedures in the protocol.

    b. The PI will maintain the following:

        i. Current curriculum vitae (CV

        ii. Protocol

        iii. Records of receipt and disposition of drugs

        iv. List of any co-investigators with their curriculum vitae

        v. Certification that all physicians, dentists, and/or nurses responsible in the study have appropriate valid licenses for the duration of the investigation, and

        vi. Case histories with particular documentation on evidence of drug effects. Emphasis is on toxicity and possible untoward happenings. All unexpected adverse effects are reportable; even if the investigator considers that the event is not related to the drug. All unexpected adverse effects shall be reported immediately to Pharmacy Service and the IRB in the manner defined by the protocol.

        vii. IRB letters of approval.

        viii. Other documents as outlined in the Human Subject Protection Program Standard Operating Procedures.

6. For research involving investigational devices:

    a) 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.

    b) If the PI is storing the devices, he/she must maintain a log indicating the identification/serial number of the device, name of subject, date dispensed, by whom it was dispensed, and amount remaining.

    c) The PI will maintain the following:

i. Current curriculum vitae (CV),
ii. Protocol of the study,
iii. Records of animal study reports
iv. Records of receipt and disposition of devices
v. List of any co-investigators with their curriculum vitae,
vi. Certification that all physicians, dentists, and/or nurses responsible in the study have appropriate valid licenses for the duration of the investigation,
vii. Case histories with particular documentation on evidence of effects. Emphasis is on safety and possible untoward happenings. All adverse device effects are reportable
viii. IRB letters of approval and any other institutional approvals required if applicable.
ix. Device training records.
x. Other documents as outlined in the Human Subject Protection Program Standard Operating Procedures.

d) Following completion of the study if the devices are kept by the pharmacy, the same termination procedure for investigational drugs must be applied. If the devices are kept by the investigator the device accountability log must be completed regarding the receipt, use and/or dispensing of the device and the disposition of remaining devices at the conclusion of the investigation.

e) If, after use, the PI keeps the devices, he/she must maintain a log regarding the receipt, use and/or re-dispensing of the device and the disposition of remaining devices at the conclusion of the investigation.

f) The PI will submit to the sponsor and to the IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.

7. When a PI files an IND or IDE, the PI is considered the sponsor and as such is accountable for all of the FDA regulatory responsibilities and reporting obligations of both the PI and the sponsor, as described in the FDA regulations. The Research Plan asks the PI if he/she also acts as the sponsor of the research and, if so, asks him/her to affirm that he/she has reviewed the Guidance Document on Requirements of the Sponsor and the Investigator as a Sponsor and will comply with the regulatory responsibilities of a sponsor. The Human Subject Protection Program will conduct education programs for investigators holding an IND or IDE on the sponsor regulations and periodically conduct random audits of PIs holding an IND or IDE as per the Research Quality Improvement Program.

7.3.2.2 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 65.11).
2. For research involving investigational devices:
    a. The IRB will review the control plan and determine whether it is adequate. If the Chair determines that the IRB does not have the necessary expertise to evaluate the plan, outside consultation will be used (e.g., Biomechanical Engineering).
    b. 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 report the findings to the PI in writing. The IRB will consider the risks and benefits of the medical device compared to the risks and benefits of alternative devices or procedures.
        i. 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 (21 CFR 812.2(b)). When the IRB approves a NSR study, the approval will require that the sponsor will comply with the abbreviated IDE requirements and this will be indicated in the approval letter to the PI.
        ii. 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.
        iii. The IRB will not review protocols involving significant risk devices under expedited review.
        iv. The IRB will document in the minutes and provide written documentation to the PI of the rationale for determining whether a device is classified as NSR/SR.
        v. 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.

7.3.3 Emergency and Expanded Use Studies

7.3.3.1 Emergency Exemption from Prospective IRB Approval

HHS regulations do not permit human subjects 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. However, nothing in the HHS 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.

FDA defines emergency use as the use of an investigational drug or biological product with a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is no sufficient time to obtain IRB approval. 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 utilized.

Informed consent must be obtained in accordance with and to the extent required by 21 CFR 50. Informed consent must be documented in writing in accordance with and to the extent required by 21 CFR 50.27.

The IRB must be notified within 5 working days when an emergency exemption is used. Any subsequent use of the test article at the institution is subject to IRB review. This notification must not be construed as an approval for the emergency use by the IRB. The IRB Director or designee will review the report to verify that circumstances of the emergency use conformed to FDA regulations.

7.3.3.2 Emergency Waiver of Informed Consent

An exception under FDA regulations at 21 CFR 50.23 permits the emergency use of an investigational drug, device, or biologic without informed consent where the investigator and an independent physician who is not otherwise participating in the clinical investigation certify in writing all four of the following specific 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 form the subject's legally authorized representative;
4. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

If time is not sufficient to obtain the independent physician determination before use of the test article, the actions of the investigator must be reviewed and evaluated in writing by an independent physician within 5-6 working days. The IRB must be notified within 5 working days when an emergency waiver is used. This notification must not be construed as an approval for the emergency waiver by the IRB. The IRB Director or designee will review the report to verify that circumstances of the emergency waiver conformed to FDA regulations.

7.3.3.3 Expanded Access of Investigational Drugs

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

1. Compassionate Use: The term “compassionate use” is erroneously used to refer to the provision of investigational drugs outside of an ongoing clinical trial to a limited number of patients who are desperately ill and for whom no standard alternative therapies are available. The term “compassionate use” does not, however, appear in FDA or HHS regulations. It is preferable, instead, to use the names of the specific access programs when discussing the use of investigational articles outside of formal clinical trials.
2. Group C Treatment Investigational New Drug (IND): A means for the distribution of investigational drugs, agents, or biologics to oncologists for the treatment of cancer under protocols outside controlled clinical trials. Group C drugs, agents, or biologics usually have shown evidence of relative and reproducible efficacy in a specific tumor type. Although the FDA typically grants a waiver for most drugs used in Group C Treatment IND protocols, the Rutgers IRB requires prospective IRB review and approval.
3. Open – Label Protocol: A study designed to obtain additional safety data, typically done when the controlled trial has ended and treatment continues. The purpose of such a study is to allow subjects to continue to receive the benefits of the investigational drug, agent, or biologic until marketing approval is obtained. Prospective IRB review and approval is required.
4. Parallel Track: A method approved by the FDA that expands the availability of investigational drugs, agents, or biologics as quickly as possible to persons with AIDS and other HIV-related diseases. These drugs, agents or biologics are utilized in separate protocols that “parallel” the controlled clinical trials and are essential to establish the safety and effectiveness of these new drugs, agents, or biologics. Although the Secretary of the Department of Health and Human Services may, on a protocol-by-protocol basis, waive the provisions of 45 CFR Part 46 where adequate protections are provided through other mechanisms, prospective IRB review and approval is required by the Rutgers IRB.
5. Treatment IND or Biologics: A mechanism for providing eligible subjects with investigational drugs (as early in the drug development process as possible) for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. The FDA defines an immediately life-threatening disease as a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. The FDA will permit an investigational drug to be used under a treatment IND after sufficient data have been collected to show that the drug “may be effective” and does not have unreasonable risks. Prospective IRB review and approval is required.
    a. There are four requirements that must be met before a treatment IND can be issued:
        i. The drug is intended to treat a serious or immediately life-threatening disease;
        ii. There is no satisfactory alternative treatment available;

iii. The drug is already under investigation or trials have been completed; and

iv. The trial sponsor is actively pursuing marketing approval.

b. The FDA identifies two special considerations when a patient is to be treated under a Treatment IND:

i. Informed Consent. Informed consent is especially important in treatment use situations because the subjects are desperately ill and particularly vulnerable. They will be receiving medications which have not been proven either safe or effective in a clinical setting. Both the setting and their desperation may work against their ability to make an informed assessment of the risk involved. Therefore, the IRB should ensure that potential subjects are fully aware of the risks involved in participation.

ii. Charging for Treatment INDs. The FDA permits charging for the drug, agent, or biologic when used in a Treatment IND. Therefore, the IRB Committee should pay particular attention to Treatment INDs in which the subjects will be charged for the cost of the drugs. If subjects will be charged for use of the test article, economically disadvantaged persons will likely be excluded from participation. Charging for participation may preclude economically disadvantaged persons as a class from receiving access to test articles. The IRB should balance this interest against the possibility that unless the sponsor can charge for the drug, it will not be available for treatment use until it receives full FDA approval.

6. Single-Patient Use: The use of an investigational drug outside of a controlled clinical trial for a patient, usually in a desperate situation, who is unresponsive to other therapies or in a situation where no approved or generally recognized treatment is available. There is usually little evidence that the proposed therapy is useful, but may be plausible on theoretical grounds or anecdotes of success. Access to investigational drugs for use by a single, identified patient may be gained either through the sponsor under a treatment protocol, or through the FDA, by first obtaining the drug from the sponsor and then submitting a treatment IND to the FDA requesting authorization to use the investigational drug for treatment use. Prospective IRB review and approval is required (See 5 above).

7. Emergency IND: The emergency use of an unapproved investigational drug, agent, or biologic requires an emergency IND. The FDA has established mechanisms and guidance for obtaining an Emergency IND for the use of investigational drugs, agents, or biologics.

7.3.3.4 Emergency Waiver of IND

FDA regulations at 21 CFR 312.34, 312.35, and 312.36 address the need for an investigational drug to be used in an emergency situation that does not allow time for submission of an IND. The FDA may authorize shipment of the drug for a specific use in such a circumstance in advance of submission of an IND. Prospective IRB review is required unless the conditions for exemption are met (21 CFR 56.104(c) and 56.102(d)). Informed consent is required unless the conditions for exemption are met (21 CFR 50.23). All applicable regulations must be met including those at 21 CFR Parts 50 and 56, and 21 CFR 312.34 and 312.35.

7.3.3.5 Expanded Access of Investigational Devices

1. Compassionate Use (or Single Patient/Small Group Access). The compassionate use provision allows access for patients who do not meet the requirements for inclusion in the clinical investigation but for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition. This provision is typically approved for individual patients but may be approved to treat a small group. It must be a serious disease or condition and no alternative treatment available. Prior FDA approval is needed before compassionate use occurs.
2. Treatment Use. An approved IDE specifies the maximum number of clinical sites and the maximum number of human subjects that may be enrolled in the study. During the course of the clinical trial, if the data suggests that the device is effective, then the trial may be expanded to include additional patients with life-threatening or serious diseases. The criteria include:
    a. Life-threatening or serious disease
    b. No alternative
    c. Controlled clinical trial
    d. Sponsor pursuing marketing approval
3. Continued Access. FDA may allow continued enrollment of subjects after the controlled clinical trial under an IDE has been completed in order to allow access to the investigational medical device while the marketing application is being prepared by the sponsor or reviewed by FDA. There must a public health need or preliminary evidence that the device will be effective and there are no significant safety concerns.

7.3.3.6 Humanitarian Use Devices (HUD)

In accordance with 21 CFR 814.124, treatment with a HUD is subject to full board initial and continuing review by the IRB. At the time of review, the IRB will determine if written consent from participants for use of the HUD is necessary. If a physician in an emergency situation determines that IRB approval cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be administered without prior IRB

approval. In this instance, approval must be obtained from the Chief of Staff and the investigator is required to provide written notification of the use to the IRB within five days after use of the device. The IRB requires that written notification include identification (specification without identifiers) of the patient, the date on which the device was used, and the reason for the use. It is the responsibility of the investigator to notify the FDA if the IRB were ever to withdraw approval for use of a HUD. The FDA should be notified within five days of notification of the withdrawal of approval. Investigators are reminded that Humanitarian Device Exemptions are for clinical use only and HUDs can be used only for purposes outlined in the approved IRB application.

7.3.3.7 Waiver of Informed Consent for Planned Emergency Research

Rutgers IRB follows FDA regulations, 21 CFR 50.24, and any applicable state requirements which permit waiver of informed consent requirements for emergency research when human subjects in need of emergency medical intervention cannot provide legally effective informed consent and their legally authorized representatives (LARs) are also unable or unavailable to give informed consent on their behalf.

8 Unanticipated Problems Involving Risks to Subjects or Others

Rutgers 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.

The following procedures describe how unanticipated problems involving risk to subjects or others are handled in research under the auspices of Rutgers.

8.1 Definitions

Unanticipated problems involving risk to participants or others refer to any incident, experience, outcome, or new information that:

1. Is unexpected
2. Is related or possibly related to participation in the research, and
3. 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.

Unexpected. The incident, experience or outcome is not expected (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;

Related. There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

Adverse Event. An adverse event is defined as 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.

8.2 Procedures

8.2.1 Reporting

Investigators must promptly report the following problems to the IRB:

1. Adverse events involving direct harm to participants which in the opinion of the principal investigator meet the criteria for an unanticipated problem involving risk to subjects or others.
2. An unanticipated event related to the research that exposes participants to potential risk but that does not involve direct harm to participants.
3. An unanticipated event related to the research that exposes individuals other than the research participants (e.g., investigators, research assistants, students, the public, etc.) to potential risk

4. IND Safety Reports from sponsors that meet the criteria for an unanticipated problem involving risk to subjects.
5. New information that indicates a change to the risks or potential benefits of the research. For example:
    a. 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.
    b. A paper is published from another study that shows that the risks or potential benefits of your research may be different than initially presented to the IRB.
6. A breach of confidentiality.
7. Incarceration of a participant in a protocol not approved to enroll prisoners,
8. Changes increasing the risk to subjects and/or affecting significantly the conduct of the trial
9. Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant.
10. Complaint of a participant 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 participants or others or that indicates participants or others may be at increased risk of harm.
12. Sponsor imposed suspension Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
13. Any other event that indicates participant or others might be at risk of serious, unanticipated harms that are reasonably related to the research.

8.2.2 Submission of Reports

Investigators must report possible unanticipated problems to the IRB promptly.

Timeframe for reporting:

REPORT WITHIN 24 HOURS OF DISCOVERY a death in an interventional study for which a RUTGERS IRB is the IRB of record, whether or not considered study-related:

REPORT WITHIN ONE WEEK OF DISCOVERY an unanticipated problem which is a serious adverse event:

REPORT WITHIN TWO WEEKS OF DISCOVERY all other unanticipated problems:

Investigators or the study team must report possible unanticipated problems to the IRB Office in writing using the Unanticipated Problem Reporting Form. The written report should contain the following:

a. Detailed information about the possible unanticipated problems, including relevant dates.
b. Any corrective action, planned or already taken, to ensure that the possible unanticipated problems is corrected and will not occur again.
c. An assessment of whether any subjects or others were placed at risk as a result of the event or suffered any physical, social, or psychological harm and any plan to address these consequences.
d. Any other relevant information.
e. Any other information requested by the IRB Office.

A report of a possible unanticipated problem involving risks to participants or others will be immediately forwarded by IRB Office staff to the IRB Chair if the IRB Office staff believes that immediate intervention may be required to protect participants or others from serious harm.

Upon receipt of a report of a possible unanticipated problem from someone other than the investigator or study staff, the IRB director will notify the PI on the study when appropriate.

8.2.3 IRB Procedures for Handling Reports of Possible Unanticipated Problems

8.2.3.1 Review by IRB Staff and Chair

1. Upon receipt of an Unanticipated Event Reporting Form from a Principal Investigator, the IRB support staff checks the form for completeness. If any applicable sections of the form are incomplete or have been answered unsatisfactorily, the IRB staff will contact the investigator or the designated contact person to obtain additional information. Corrections are documented in the IRB file, indicating the date, the person spoken with, and the IRB staff making the correction.
2. The IRB chairperson and/or other experienced member(s) designated by the IRB chairperson receive and reviews the report of the event(s) considered to be an unanticipated problem. The IRB chairperson (or designee) will make the final determination as to whether the event is to be regarded as an unanticipated problem.
3. Based on the information received from the investigator, the IRB Chair or designee may suspend research to ensure protection of the rights and welfare of participants. Suspension directives made by the IRB Chair or designee must be reported to a meeting of the convened IRB.
4. The IRB or the IRB chairperson (or designee) has authority to require submission of more detailed contextual information by the PI, the sponsor, the study coordinating

center, or DSMB/DMC about any adverse event occurring in a research protocol as a condition of the continuation of the IRB's approval of the research.

5. If the reviewer considers that either (1) the problem was foreseen OR (2) no participants or others were harmed AND participants or others are not at increased risk of harm, the reviewer indicates on the form that the problem is not an unanticipated problem. The form is filed in the protocol record, the determination is communicated to the investigator and no further action is taken.
6. If the reviewer considers that the problem is an unanticipated problem, but that the risk is no more than minimal, the reviewer will review:
    a. The currently approved protocol
    b. The currently approved consent document
    c. Previous reports of unanticipated problems involving risks to participants or others
    d. The investigator's brochure, if one exists

    After reviewing all of the materials, the reviewer will take appropriate action depending on the nature of the risk involved, including requiring modification of the protocol or the consent form, if applicable. The results of the review will be recorded in the protocol record, communicated to the investigator, and reported to the IRB. All events determined to be unanticipated problems will be reported to the relevant regulatory agencies and institutional officials.
7. All reported unanticipated problems where the risk is more than minimal will be reviewed at a convened IRB meeting.

8.2.3.2 IRB Review

For the convened IRB meeting, the primary reviewer will be given the protocol file, the currently approved consent document, previous reports of unanticipated problems involving risks to participants or others, the investigator's brochure (if one exists), the event report, and recommendations from the IRB Chair or designee, when appropriate. All IRB members will receive the event report.

After review of the protocol and event report, the full IRB will make findings and recommendations based on the following considerations:

a. Whether the reported event is an unanticipated problem involving risks to participants or others according to the definition in this policy.
b. What action in response to the report is appropriate.
c. Whether suspension or termination of approval is warranted.
d. Whether further reporting to Institutional and/or federal officials is required.

1. If the IRB finds that the event is not an unanticipated problem involving risks to participants or others, according to the definition in the policy, the IRB may recommend any of the following actions:

a. No action
b. Requiring modifications to the protocol
c. Revising the continuing review timetable
d. Modifying the consent process
e. Modifying the consent document
f. Providing additional information to current participants (e.g. whenever the information may relate to the participant's willingness to continue participation)
g. Providing additional information to past participants
h. Requiring additional training of the investigator and/or study staff
i. Other actions appropriate for the local context

2. If the IRB finds that the event is an unanticipated problem involving risks to participants or others, according to the definition in the policy, the IRB may recommend any of the following actions:
    a. Requiring modifications to the protocol
    b. Revising the continuing review timetable
    c. Modifying the consent process
    d. Modifying the consent document
    e. Providing additional information to current participants (e.g. whenever the information may relate to the participant's willingness to continue participation)
    f. Providing additional information to past participants
    g. Requiring additional training of the investigator and/or study staff
    h. Reconsidering approval
    i. Requirement that current participants re-consent to participation
    j. Monitoring of the research
    k. Monitoring of the consent
    l. Referral to other Institutional entities (e.g., legal counsel, risk management, institutional official)
    m. Suspending the research
    n. Terminating the research
    o. Other actions appropriate for the local context
3. If a report suggests that participant safety is at risk, the IRB may immediately suspend or terminate the research. Any suspension or termination of research by

the IRB must be promptly reported to the Vice President for Research, and OHRP, and FDA (if FDA-regulated research). This should be done in writing.

4. If, after reviewing a report, the IRB finds that the event is an unanticipated problem involving risks to participants or others or that suspension or termination of approval is warranted, the IRB will:
    a. Notify the investigator in writing of its findings, with copies to the Chair of the investigator's department and/or research unit, other affected units and the investigator's supervisor, and
    b. Report its findings and recommendations to the Vice President for Research for further reporting to the appropriate federal officials

8.3 Non-Reportable Events

The IRB recognizes that sponsors may require that the PI report all serious adverse events and IND safety reports to the IRB. The IRB complies with this request in an efficient manner to acknowledge receipt of these reports.

The PI's may report adverse events and IND safety reports that do not meet the above reporting requirements in summary form at the time of continuing review.

9 Protocol Deviations

It is the policy of Rutgers IRB to be notified of any protocol deviations or violations that result in an increase in risk or a decrease in benefit to participants.

The following procedures describe how protocol deviations are reported to the IRB.

9.1 Definitions

Deviations. A protocol deviation is defined as a violation that is unanticipated and happens without any prior agreement (protocol visit scheduled outside protocol window, blood work drawn outside protocol window, etc.). The IRB will review these reports for frequency and may audit any protocol reporting frequent deviations.

9.2 Deviations

Protocol deviations are 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 the IRB Office as soon as possible / Protocol Deviation Form.
- are reviewed to determine if they:
    - Are minor, and don't impact subject safety (these are acknowledged by the IRB)
    - Constitute noncompliance. In these cases, the deviations would be reviewed by the IRB for determination of non-serious, serious, or continuing noncompliance; the latter two must be reported to OHRP, and other federal agencies (e.g., FDA etc.) and sponsors (as applicable).
    - 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 are reported to OHRP, and other federal agencies (e.g., FDA etc.) and sponsors (as applicable). See section 8 for additional information on UPs.

When a sponsor requests that the IRB be notified of a deviation, the completed form will be forwarded to the IRB chair or designate for review of the "Protocol Deviation Report" form submitted by the Investigator.

9.3 Reporting & Review

Deviation Report forms are to be completed for those events that qualify as a protocol deviation. These reports should be filed with the IRB Office. The IRB Office will forward the report to the IRB Chair or designee for review and signature. The IRB Chair or

designee may choose to place any deviation on the agenda of the next convened IRB meeting for discussion and further action if necessary.

10 Complaints and Non-compliance

As part of its commitment to protecting the rights and welfare of human subjects in research, Rutgers reviews all complaints and allegations of non-compliance and takes any necessary action to ensure the ethical conduct of research.

All Investigators and other study personnel involved in human subjects research are required to comply with all laws and regulations governing their research activities, as well as with requirements and determinations of the IRB. Study personnel include the Principal Investigator and any staff member directly involved with participants or the informed consent process or their identifiable data.

The following procedures describe how complaints and allegations of non-compliance are handled by the IRB.

10.1 Definitions

Non-compliance. Non-compliance is defined as failure to comply with any of the regulations and policies described in this document and 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. Serious non-compliance is defined as failure to follow any of the 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 participants, decreases potential benefits, or compromises the integrity of the human research protection program. 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 considered serious noncompliance.

Continuing non-compliance. Continuing non-compliance is defined as 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. Continuing non-compliance also includes failure to respond to a request to resolve an episode of non-compliance.

Allegation of Non-Compliance. Allegation of Non-Compliance is defined as an unproved assertion of non-compliance.

Finding of Non-Compliance. Finding of Non-Compliance is defined as an allegation of non-compliance that is proven true or a report of non-compliance that is clearly true. (For example, 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

10.2 Complaints

The Chair of the IRB will promptly handle (or delegate staff to handle), and, if necessary, investigate all complaints, concerns, and appeals received by the IRB. This includes complaints, concerns, and appeals from investigators, research participants and others.

All complaints, written or verbal (including telephone complaints), and regardless of point of origin, are recorded on a complaint intake form and forwarded to the Chief HSPP, IRB Chair and IRB Director.

10.3 Non-compliance

Investigators and their study staff are required to report instances of possible non-compliance. The Principal Investigator is responsible for reporting any possible non-compliance by study personnel to the IRB. Common reports to the IRB that are not serious or continuing are typically protocol violations. However, any individual or employee may report observed or apparent instances of noncompliance Rutgers IRB. In such cases, the reporting party is responsible for making these reports in good faith, maintaining confidentiality and cooperating with any 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 IRB Chair, IRB Director, or HSPP Chief directly to discuss the situation informally.

Reports of non-compliance must be submitted to the IRB Office within a timely manner of discovery of this noncompliance. The report must include a complete description of the noncompliance, the personnel involved and a description of the non-compliance.

Complainants may choose to remain anonymous.

10.3.1 Review of Allegations of Non-compliance

All allegations of non-compliance will be reviewed by the IRB Full Board Committee, who will review:

1. All documents relevant to the allegation
2. The last approval letter from the IRB
3. The last approved IRB application and protocol;
4. The last approved consent document
5. The grant, if applicable; and
6. Any other pertinent information (e.g., questionnaires, DSMB reports, etc.).

The IRB Committee will review the allegation and they may request additional information or an audit of the research in question.

When the Committee determines 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 if applicable the reporting party. The determination letter will be copied to the Institutional Official in cases where the Institutional Official and any other parties had been notified at the outset.

If in the judgment of the IRB Committee, the reported allegation of non-compliance is true, the non-compliance will be processed according to Section 9.4.2 Review of Findings of Non-compliance.

If in the judgment of the IRB Committee, any allegation or findings of non-compliance warrants suspension of the research before completion of any review or investigation to ensure protection of the rights and welfare of participants, the IRB Committee may suspend the research with subsequent review by the IRB.

The Committee may determine that additional expertise or assistance is required to make these determinations and may form an ad hoc committee to assist with the review and fact gathering process. When an ad hoc committee assists in the review process, the Committee is responsible for assuring that minutes of the meeting are generated and kept to help support any determinations or findings made by the ad hoc committee.

10.3.2 Review of Findings of Non-compliance

Noncompliance that is not serious or continuing:

When the IRB Committee 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. The Committee will work with the PI to develop a corrective action plan to prevent future noncompliance.

Serious or Continuing Noncompliance

When the IRB Committee determines that noncompliance has occurred

, the IRB may:

1. Find that there is noncompliance that is neither serious nor continuing and an adequate corrective action plan is in place
2. Find that there is serious or continuing non-compliance and approve any changes proposed by the Chair and/or ad hoc committee
3. Find that there may be serious or continuing non-compliance and direct that a formal inquiry (described below) be held; or
4. Request additional information.

10.3.3 Inquiry Procedures

A determination may be made by the IRB that an inquiry is necessary based on several issues that may include but are not limited to:

1. Subject(s)' complaint(s) that rights were violated;
2. Report(s) that investigator is not following the protocol as approved by the IRB;
3. Unusual and/or unexplained adverse events in a study;
4. Repeated failure of investigator to report required information to the IRB.

The inquiry will be conducted by the HSPP QA team. The inquiry can include any or all of the following:

1. Review of protocol(s) in question;
2. Review of sponsor audit report of the investigator, if appropriate;
3. Review of any relevant documentation, including consent documents, case report forms, subject's investigational and/or medical files etc., as they relate to the investigator's execution of her/his study involving human subjects;
4. Interview of appropriate personnel if necessary;
5. Preparation of either a written or oral report of the findings, which is presented to the full IRB at its next meeting;
6. Recommend actions if appropriate.

10.3.4 Final Review

The results of the inquiry will be reviewed at a convened IRB meeting where the IRB will receive a report from the HSPP QA team. If the results of the inquiry substantiate the finding of serious or continuing non-compliance, the IRB's possible actions could include, but are not limited to:

1. Request a correction action plan from the investigator
2. Verification that participant selection is appropriate and observation of the actual informed consent
3. An increase in data and safety monitoring of the research activity
4. Request a directed audit of targeted areas of concern
5. Request a status report after each participant receives intervention
6. Modify the continuing review cycle
7. Request additional Investigator and staff education
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 participants 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 and is given a chance to respond. If the IRB determines that the non-compliance was serious or continuing, the results of the final review will be reported as described below..

11 Reporting to Regulatory Agencies and Institutional Officials

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 IRB approval. Rutgers will comply with this requirement and the following procedures describe how these reports are handled.

11.1 Procedures

1. IRB staff will initiate these procedures as soon as the IRB takes any of the following actions:

   a. Determines that an event may be considered an unanticipated problem involving risks to participants or others

   b. Determines that non-compliance was serious or continuing

   c. Suspends or terminates approval of research

2. The Director or designee is responsible for preparing reports or letters which includes the following information:

   a. The nature of the event (Unanticipated problem involving risks to participants or others, serious or continuing non-compliance, suspension or termination of approval of research)

   b. Name of the institution conducting the research

   c. Title of the research project and/or grant proposal in which the problem occurred

   d. Name of the principal investigator on the protocol

   e. Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement)

   f. A detailed description of the problem including the findings of the Institution and the reasons for the IRB's decision

   g. 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.)

   h. Plans, if any, to send a follow-up or final report by the earlier of

      1. A specific date

      2. When an investigation has been completed or a corrective action plan has been implemented

3. The HSPP Chief, and when warranted Legal Counsel, review the letter/report as needed

5. The IRB Director or designee sends a copy of the report to:

   a. The Institutional Official
   b. The following federal agencies:
      - OHRP, if the study is subject to DHHS regulations or subject to a DHHS Federalwide assurance
      - FDA, if the study is subject to FDA regulations.
      - If the study is conducted or funded by any Federal Agency other than DHHS that is subject to “The Common Rule”, the report is sent to OHRP or the head of the agency as required by the agency
      - 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 Institution, and the agency has been notified of the event by the investigator, sponsor, another Institution, or other mechanisms.
   c. The Associate VP for Research Administration
   d. For RBHS schools: the VP for Research and the appropriate Research Dean
   e. The Director of the Office of Research Regulatory Affairs
   f. Sponsor, if the study is sponsored
   g. The Privacy Officer of a covered entity, if the event involved unauthorized use, loss, or disclosure of individually-identifiable patient information from that covered entity
   h. Others as deemed appropriate by the Institutional Official

The Director ensures that all steps of this policy are completed in a timely manner. For more serious actions, the Director will expedite reporting.

12 Investigator Responsibilities

Principal Investigators are ultimately responsible for the conduct of research. Principal Investigators may delegate research responsibility. However, investigators 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 participants.

12.1 Investigators

Principal Investigators

12.2 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:
    1. Access to a population that would allow recruitment of the required number of subjects.
    2. Sufficient time to conduct and complete the research.
    3. Adequate numbers of qualified staff.
    4. Adequate facilities.
    5. A process to ensure that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions.
    6. 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 under the laws of New Jersey and the policies of Rutgers ;
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 ensuring that no human subject is involved in the research prior to obtaining their consent;
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 institution 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 commencement of the research;
16. Comply with all IRB decisions, conditions, and requirements;
17. Ensure that protocols receive timely continuing IRB review and approval;
18. Report unanticipated problems involving risk to subjects or other and any other reportable events to the IRB (see Section 8)
19. Obtain IRB review and approval in writing before changes are made to approved protocols or consent forms
20. Seek IRB assistance when in doubt about whether proposed research requires IRB review

12.3 Training / Ongoing Education of Investigators and Research Team

As stated above, one component of a comprehensive human research protection program is an education program for all individuals involved with research subjects. Rutgers 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.

.

12.3.1 Initial Education

The PI and key investigators must complete an IRB-approved online course in the Protection of Human Research Subjects.

New research protocols and applications for continuing review will not be accepted from principal investigators who have not completed the initial education requirement.

While research protocols and applications for continuing review will be accepted and reviewed if the Principal Investigator holds a current certification of training, final approval will not be granted until all co-investigators and members of the research team have completed the initial education requirement.

Acceptance of Alternative Education Programs

If investigators or members of their research team can verify that they have successfully completed human subjects research training equivalent to that required by Rutgers, they may request an acceptance of an alternative education program.

12.3.2 Continuing Education and Recertification

All investigators and members of their research teams certified under CITI must meet Rutgers continuing education requirement every three (3) years for as long as they are involved in human subject research. Acceptable training includes appropriate refresher modules at the CITI web-based training site.

Investigators must submit evidence of continuing education prior to the expiration of their training certification. New research protocols and applications for continuing review will not be accepted from principal investigators who have not submitted satisfactory evidence of continuing education.

Investigators who are also IRB Chair, IRB members, or IRB Office staff will satisfy the training requirements for IRB members and staff.

12.4 Investigator Concerns

Investigators who have concerns or suggestions regarding Rutgers' human research protection program should convey them to the Chief HSPP, the Institutional Official or other responsible parties (e.g. college dean, departmental Chair) regarding the issue, when appropriate. The Chief 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 Chair of the IRB or the IRB Director will be available to address investigators' questions, concerns and suggestions.

13 Sponsored Research

It is Rutgers policy that any sponsored research conducted under the auspices of the Institution 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.

13.1 Definitions

Sponsor. Sponsor means the company, institution, individual donor, or Institution responsible for the initiation, management or financing of a research study.

Sponsored research. Sponsored research means 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.

13.2 Responsibility

1) Sponsor contracts that are reviewed by the Office of Sponsored Projects
   a) The Office of Sponsored Programs will review contracts and the IRB and Office of Sponsored Programs will share contract and study information as necessary for each sponsored protocol to ensure that protocol, consent, and contract language are consistent.
2) Sponsor contract NOT reviewed by the Office of Sponsored Programs:
   a) When a contact is not reviewed by Sponsored Projects, but is reviewed by another entity in which the investigator reports, the IRB application requests a copy of the contract to ensure that the protocol, consent and contract is consistent.
3) Contracts will be reviewed for the following by both the Office of Sponsored Programs and the IRB:
   a) All sponsor contracts will indicate that Rutgers will follow the protocol, applicable regulations and its ethical standards.
   b) All sponsor contracts will define who will be responsible for research related injuries.
   c) 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 participants 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.
   d) If the sponsor discovers results that could affect the safety or medical care, the sponsor will make sure the IRB is notified.
   e) Payment in exchange for referrals of prospective participants from researchers (physicians) ("finder's fees") is not permitted. Similarly payments designed to accelerate recruitment that are tied to the rate or timing of enrollment ("bonus payments") are also not permitted.

14 Conflict of Interest in Research

It is Rutgers policy to preserve public trust in the integrity and quality of research at the Institution by minimizing actual or perceived conflict of interest in the conduct of research.

The following describe the procedures by which this responsibility is carried out.

14.1 Definitions

Conflict of Interest. A conflict of interest (COI) occurs when any financial arrangement, situation or action affects or is perceived to exert inappropriate influence on the design, review, conduct, results or reporting of research activities or findings.

Ownership interest. Ownership interest means any ownership interest, stock options, or other financial interest whose value cannot be readily determined through reference to public prices (generally, interests in a non-publicly traded corporation), or any equity interest in a publicly traded corporation during the time the investigator is carrying out the study and for 1 year following completion of the study.

Compensation. Compensation means payments made by an Institution to the investigator or the institution exclusive of the costs of conducting the research during the time the investigator is carrying out the study and for 1 year following the completion of the study. This includes, but is not limited to:

- Income from seminars, lectures or teaching engagements
- Income from service on advisory committees or review panels
- Grants to fund ongoing research
- Compensation in the form of equipment
- Retainers for ongoing consultation

Patent. A patent is an official written document securing to an inventor for a term of years the exclusive right to make, use, or sell an invention.

Royalty. A royalty is compensation for an invention.

Immediate Family Member. Immediate family member: having a relationship to a person (whether by blood, law, or marriage) as a spouse, parent, child, grandparent, grandchild, stepchild, or sibling.

Financial Interest Related to the Research. Financial Interest Related to the Research means financial interest in the sponsor, product or service being tested, or competitor of the sponsor or product or service being tested.

Significant Financial Interest. Significant Financial Interest includes:

- Ownership interest, stock options, or other financial interest related to the research unless it meets four tests:
    - Less than $5,000 when aggregated for the immediate family.

    - Publicly traded on a stock exchange.
    - Value will not be affected by the outcome of the research.
    - Less than 5% interest in any one single entity.
- Compensation related to the research unless it meets two tests:
    - Less than $5,000 in the past year when aggregated for the immediate family.
    - Amount will not be affected by the outcome of the research.
- Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.
- Board or executive relationship related to the research, regardless of compensation.

Non-financial Conflict of Interest. Non-financial conflict of interest may exist when an individual serves dual roles, such as health care provider and investigator. Other interests such as publication, promotion or tenure, can also become conflicts of interest that may affect an individual's judgment. Membership in oversight committees such as the IRB as well as positions of authority may pose potential conflicts of interest. Any position that includes responsibilities for the review and approval of research projects or contracts other than his/her own may potentially affect the design of, decisions made and/or action taken surrounding a specific study.

Key Personnel. Key research personnel are those individuals who: 1) obtain consent from human subjects; 2) recruit human subjects; or 3) evaluate the response of human subjects.

14.2 Individual Conflicts of Interest

These procedures apply to both financial and non-financial conflicts of interest and are guided by Code of Federal Regulations (Title 42 of the Code of Federal Regulations (CFR) Part 50 Subpart F) that promotes objectivity in research to ensure conflict of interests do not adversely affect the protection of participants or the credibility of Rutgers Human Research Protection Program (HSPP).

For clinical studies involving the use of new 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.

In the environment of research, openness and honesty are indicators of integrity and responsibility, characteristics that promote quality research and can only strengthen the research process. Therefore, conflicts of interest should be eliminated when possible and effectively disclosed and managed when they cannot be eliminated.

14.2.1 Procedures

14.2.1.1 Disclosure of Investigator COI

The IRB application asks that the PI and study personnel with access to subjects or their personal information disclose any financial or other personal interest per institutional policy.

14.2.1.2 Evaluation of COI

At initial review of the research protocol and COI disclosure, the IRB also determines the following:

- Whether the conflict, financial or non-financial, affects the protections of research participants,
- Whether a conflicting interest might adversely affect the credibility of the HSPP thus creating the appearance of conflicts of interest.

Points to consider are:

- How is the research supported or financed,
- By whom the study is designed,
- Will the institution receive any compensation, and if the institution is an appropriate site for the research.

14.2.1.3 Management of COI

The IRB will determine if the rights and welfare of human research participants will be better protected by any or a combination of the following:

1. Disclosure to subjects through the consent process
2. Modification of the research protocol or safety monitoring plan
3. Monitoring of research by independent reviewers
4. Disqualification of the conflicted party from participation in all or a portion of the research
5. Appointment of a non-conflicted Principal Investigator
6. Divestiture of significant financial interests
7. Severance of relationships that create actual or potential conflicts.
8. Prohibition of the conduct of the research at the Institution

14.3 Recruitment Incentives

Payment arrangements among sponsors, Institutions, investigators, and those referring research participants may place participants at risk of coercion or undue influence or cause inequitable selection. Payment in exchange for referrals of prospective

participants from researchers (physicians) (“finder’s fees”) is not permitted. Similarly payments designed to accelerate recruitment that is tied to the rate or timing of enrollment (“bonus payments”) are also not permitted.

14.4 Institutional Conflict Of Interest

These procedures apply to all human subjects research conducted at Rutgers. This policy applies to investigators, IRB members and staff, and institutional officials.

The policy of Rutgers is to ensure that the welfare of human subjects and the integrity of research will not be compromised, or appear to be compromised, by competing institutional interests or obligations. Although Rutgers policy has separated technology transfer functions from research administration, circumstances may exist in which separation of function is not sufficient to avoid the appearance of institutional conflict of interest.

Institutional financial interests may be created by gifts, payments, royalty income, equity, and other benefits from or interests in for-profit Institutions. Institutional financial interests also are created by financial and fiduciary interests of Institutional Officials.

14.4.1 Responsibilities

The Conflict of Interest Committee (COIC) will be responsible for evaluating potential institutional conflict of interest and will take actions as required to avoid, or to appropriately manage, apparent institutional COI. These actions may involve referral to appropriate advisors outside the facility or obtaining advisement from the Institution Counsel. If used, outside advisors will be individuals who have sufficient seniority, expertise, and independence to evaluate the competing interests at stake and to make credible and effective recommendations. All outside advisors will be independent of the management of oversight for the Human Research Protection Program (HSPP) within the institution. The utilization of outside advisors will increase the transparency of the deliberations and enhance the credibility of determinations.

After reviewing a significant financial interest in research, the COIC will communicate its conclusions, along with any management arrangements to be imposed, to the IRB. All relevant conflicts will be disclosed to research participants in a form to be determined by the IRB. The COIC also will communicate conclusions and COI management strategies to the Institutional Official and the PI.

15 Health Insurance Portability and Accountability Act (HIPAA)

Protected Health Information obtained by Rutgers may not be used internally or disclosed to any outside person or Institution for research purposes without prior approval of the IRB. Rutgers researchers must also abide by all corporate HIPAA policies regarding HIPAA privacy and security.

The following describe the procedures for conducting research at OX in accordance with the Health Insurance Portability and Accountability Act (HIPAA) of 1996.

15.1 Definitions

Access. Access is the mechanism of obtaining or using information electronically, on paper, or other medium for the purpose of performing an official function.

Authorization. An authorization is 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. Covered entity is 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. Common Rule is a federal Policy on human subject protection that provides for the primary source of regulation of research.

De-Identified Information. De-Identified Information is health information that does not identify an individual and with respect to which 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 exempt from HIPAA.

Deletion. Deletion is the removal, erasing, or expunging information or data from a record.

Disclosure. Disclosure is the release, transfer, provision of access to, or divulging in any other manner information outside of the covered entity.

Health Information. Health Information is 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.

Identifiable Health Information. Identifiable Health Information is a subset of health information including demographic information collected from an individual.

Limited Data Set. Limited Data Set is 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. Minimum Necessary refers to 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 . Privacy Board is 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. Is an alternative to an IRB for privacy issues only. It cannot replace the IRB for Common Rule purposes.

Privacy Act. Privacy Act is 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. 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 participants. The IRB members should know strategies to protect privacy interests relating to contact with potential participants, and access to private information.

Protected Health Information. Protected Health Information is 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. Preparatory Research is the method applied to developing or designing a research study.

Waiver of Authorization. Waiver of Authorization is a means of requesting approval from an IRB or Privacy Board rather than asking each research subject for an authorization to access protected health information.

15.2 Historical Background

The *Health Insurance Portability and Accountability Act of 1996* (HIPAA) required the creation of a Privacy Rule for identifiable health information. The resulting Privacy Rule, finalized in August 2002, set a compliance date of April 14, 2003. While the main impact of the Privacy Rule will be on the routine provision of and billing for health care, the Rule will also affect the conduct and oversight of research. Researchers, IRB staff and members as well as research administration must be aware of these changes.

15.3 Effects of HIPAA on Research

The final Privacy Rule published on August 14, 2002 included a number of changes in how the Rule applies to research. See the NIH HIPAA Privacy Rule Booklet for Research and the NIH fact sheet on Institutional Review Boards and HIPAA for more information on how HIPAA applies to research. See also Impact of the Privacy Rule on Academic Research, a white paper published by the American Council on Education.

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 Common Rule contains specific requirements for a composition of an IRB and the Privacy Rule contains specific requirements for a Privacy Board. The composition of a Privacy Board is similar to that of an IRB.

Researchers who are working with “Protected Health Information” (PHI) will be required to comply with the rules on HIPAA. Rutgers IRB acts as the Institution’s Privacy Board.

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. For clinical trials, authorization must be sought in addition to informed consent. Authorization must also be sought for other research uses or disclosures of protected health information that do not qualify for an IRB waiver of authorization (discussed below).

The Privacy Rule has several special provisions that apply to research authorizations for uses and disclosures of PHI for research purposes. These requirements are as follows:

1. An authorization for a research purpose may state that the authorization does not expire, that there is no expiration date or event, or that the authorization continues until the end of the research study; and
2. An authorization for the use or disclosure of protected health information for research may be combined with a consent to participate in the research, or with any other legal permission related to the research study (except for research involving the use or disclosure of psychotherapy notes, which must be authorized separately); and
3. Research authorization forms must be filled out completely and accurately by the investigator, to ensure that all parties who require access to protected health information for the research (including sponsors, CROs, DSMBs, IRBs, etc.) are identified in the form and may receive the information. The IRB combined authorization/consent form should be completed by the investigator and submitted to Rutgers IRB for review and approval.

15.4 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”, separate federal

legislation designed to protect human subjects involved in research. HIPAA describes privacy standards for protecting PHI and so only applies to research that involves humans' (not animals') health information.

15.4.1 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 when presented with documentation that an 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 or Privacy Board and the date on which the alteration or waiver of authorization was approved;
2. A statement that the IRB or Privacy Board 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 or Privacy Board;
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 signature of the chair or other member, as designated by the chair, of the IRB or the Privacy Board, as applicable.

The following criteria must be satisfied for the IRB to approve a waiver of authorization under the Privacy Rule:

> *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; and
> 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.

15.4.2 Review Preparatory to Research

The Privacy Rule permits a covered entity to use or disclose protected health information to a researcher 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. Prior to permitting the researcher to access the protected health information, the covered entity must obtain representations from the researcher that the use or disclosure of the protected health information is solely to prepare a research protocol or for similar purposes preparatory to research, that the researcher will not remove any protected health information from the covered entity, and that protected health information for which access is sought is necessary for the research purpose. Researchers should consult the covered entity regarding any forms or applications necessary to conduct a review preparatory to research.

Researchers conducting a review preparatory to research may not record information in identifiable form, nor may they use the information that they receive to contact potential subjects, unless the investigator is also the subject's treating physician. Because the Privacy Rule permits a covered entity to disclose protected health information to the individual who is the subject of the information, covered health care providers and patients may continue to discuss the option of enrolling in a clinical trial without patient authorization. Even when permitted by the Privacy Rule, however, any use of patient information for recruitment must comply with IRB recruitment policies (see discussion below).

1. All human subjects research requires IRB review to determine either a) exempt status or b) need for further review.

2. Reviews preparatory to research that are permitted under HIPAA may or may not be human subjects research depending on the investigation being conducted.

    1. Only those reviews of a database by an individual entitled to access that database intended to enumerate an available data set without reviewing PHI and for which no PHI is recorded do not require review. For example: medical records may be queried for information such as: In the year XXXX how many patients had a discharge diagnosis of [indicate disease/diagnosis]. IRB Privacy Board Review is required for all other uses of PHI as indicated.
    2. If the research involves a de-identified data set, defined as removing the following identifiers, then a de-identified data set certification form must be completed submitted for administrative review and certified prior to accessing the data set. This activity also requires an IRB determined exemption from review:

1. Names
2. Geographic info. (city, state, and zip)
3. Elements of Dates (except years)
4. Telephone #s
5. Fax #s
6. E-mail address
7. Social Security#
8. Medical Record, prescription #s
9. Health Plan Beneficiary #s
10. Account #s
11. Certificate /License #s
12. VIN and Serial #s, license plate #s.
13. Device identifiers, serial #s
14. Web URLs
15. IP address #s
16. Biometric identifiers (finger prints)
17. Full face, comparable photo images
18. Unique identifying #s

IRB Privacy Board review and approval is required prior to initiating this research. Investigators are not authorized to contact potential research subjects identified in reviews preparatory to research unless they are directly responsible for care of the potential subject and entitled to PHI as a result of that duty.

Investigators, who have previously obtained full consent and authorization to contact a research subject as a result of a previously approved research project, may contact his or her former research subjects provided that the subject agreed to be contacted for information on future research conducted by the same principal investigator or co-investigator (s).

15.4.3 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 researcher 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. Researchers should submit the applicable IRB form for IRB approval when they intend to conduct research involving decedents’ protected health information.

15.4.4 Limited Data Sets with a Data Use Agreement

When a researcher does not need direct identifiers for a study but does require certain data elements that are not permitted in de-identified data, the Privacy Rule permits a covered entity to disclose a “limited data set” to the researcher without authorization or waiver, provided that the researcher has signed a data use agreement. The limited data set is still considered to be protected health information, but it must exclude only specified direct identifiers of the individual or of relatives, employers, or household members of the individual.

If the research involves a limited data set, defined as removing the following 16 identifiers:

1. Names
2. Postal address info. (if other than city, state and zip)
3. Telephone and fax #s
4. Email addresses
5. Social Security #s
6. Medical record, prescription numbers
7. Health plan beneficiary #s
8. Account #s
9. Certificate/license #s
10. Vin and serial #s, license plate #s
11. Device identifiers, serial #s
12. Web URLs
13. IP address #s
14. Biometric identifiers (finger prints)
15. 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:
4. Not to use or disclose the information other than as permitted by the data use agreement or as otherwise required by law;
5. Use appropriate safeguards to prevent the use or disclosure of the information other than as provided for in the data use agreement;
6. 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

7. Not to identify the information or contact the individual.
8. Researchers who will be receiving limited data sets must submit a signed copy of the covered entity's data use agreement to OX IRB for approval, prior to initiating the research. Transition Provisions

The Privacy Rule contains certain grandfathering provisions that permit a covered entity to use and disclose protected health information for research after the Rule's compliance date of April 14, 2003, if the researcher obtained any one of the following prior to the compliance date:

1. An authorization or other express legal permission from an individual to use or disclose protected health information for the research;
2. The informed consent of the individual to participate in the research; or
3. An IRB waiver of informed consent for the research.

Even if informed consent or other express legal permission was obtained prior to the compliance date, if new subjects are enrolled or existing subjects are re-consented after the compliance date, the covered entity must obtain the individual's authorization. For example, if there was a temporary waiver of informed consent for emergency research under the FDA's human subject protection regulations, and informed consent was later sought after the compliance date, individual authorization must be sought at the same time.

The transition provisions apply to both uses and disclosures of protected health information for specific research protocols and uses or disclosures to databases or repositories maintained for future research.

15.5 HIPAA and Documentation Requirements

HIPAA documents include an authorization form, a waiver of authorization form, and a de-identification form. One of these documents must be used whenever PHI is utilized in the research.

15.6 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.

15.7 HIPAA and Existing Studies

Any research subject enrolled in a study that uses PHI from a covered entity must sign a HIPAA-compliant authorization form. This form is in addition to the existing Informed

Consent document, and is federally required. In a few cases, the Informed Consent document may be combined with a HIPAA authorization.

15.8 Waivers to HIPAA Consent Form

In some cases Rutgers IRB may approve a waiver to use of the HIPAA authorization form. This may occur when the IRB finds that the research could not be practically done without the waiver, and not without access to and use of the PHI, and that disclosure poses minimal risk to privacy.

16 Special Topics

16.1 Certificate of Confidentiality (CoC)

Certificates of Confidentiality are issued by the federal government to protect identifiable research information from forced disclosure. They allow the investigator and others who have access to research records to refuse to disclose identifying information on research participants in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. CoCs may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation.

The certificate goes beyond the consent form in ensuring confidentiality and anonymity. Without the certificate, researchers can be required by a court-ordered subpoena to disclose research results (usually as part of a criminal investigation of the subjects).

Any research project that collects personally identifiable, sensitive information and that has been approved by an IRB is eligible for a Certificate. Federal funding is not a prerequisite for a Certificate.

16.1.1 Statutory Basis for Protection

Protection against compelled disclosure of identifying information about subjects of biomedical, behavioral, clinical, and other research is provided by the Public Health Service Act §301(d), 42 U.S.C. §241(d):

"The Secretary may authorize persons engaged in biomedical, behavioral, clinical, or other research (including research on mental health, including research on the use and effect of alcohol and other psychoactive drugs) to protect the privacy of individuals who are the subject of such research by withholding from all persons not connected with the conduct of such research the names or other identifying characteristics of such individuals. Persons so authorized to protect the privacy of such individuals may not be compelled in any Federal, State or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals."

16.1.2 Usage

Certificates of Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. By protecting researchers and institutions from being compelled to disclose information that would identify research subjects, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by assuring confidentiality and privacy to subjects.

Any investigator engaged in research in which sensitive information is gathered from human subjects (or any person who intends to engage in such research) may apply for a Certificate of Confidentiality. Research can be considered "sensitive" if it involves the collection of:

1. information about sexual attitudes, preferences, practices;

2. information about personal use of alcohol, drugs, or other addictive products;
3. information about illegal conduct;
4. information that could damage an individual's financial standing, employability, or reputation within the community;
5. information in a subject's medical record that could lead to social stigmatization or discrimination; or
6. information about a subject's psychological well-being or mental health.

This list is not exhaustive. Researchers contemplating research on a topic that might qualify as sensitive should contact the IRB Office for help in applying for a certificate.

In the informed consent form, investigators should tell research subjects that a Certificate is in effect. Subjects should be given a fair and clear explanation of the protection that it affords, including the limitations and exceptions noted above. Every research project that includes human research subjects should explain how identifiable information will be used or disclosed, regardless of whether or not a Certificate is in effect.

16.1.3 Limitations

The protection offered by a Certificate of Confidentiality is not absolute. A Certificate protects research subjects only from legally compelled disclosure of their identity. It does **not** restrict voluntary disclosures.

For example, a Certificate does not prevent researchers from voluntarily disclosing to appropriate authorities such matters as child abuse, a subject's threatened violence to self or others, or from reporting a communicable disease. However, if researchers intend to make such disclosures, this should be clearly stated in the informed consent form which research subjects are asked to sign.

In addition, a Certificate of Confidentiality does **not** authorize the person to whom it is issued to refuse to reveal the name or other identifying characteristics of a research subject if

1. the subject (or, if he or she is legally incompetent, his or her legal guardian) consents, in writing, to the disclosure of such information;
2. authorized personnel of the Department of Health and Human Services (DHHS) request such information for audit or program evaluation, or for investigation of DHHS grantees or contractors and their employees; or
3. release of such information is required by the Federal Food, Drug, and Cosmetic Act or regulations implementing that Act.

16.1.4 Application Procedures

Any person engaged in research collecting sensitive information from human research subjects may apply for a Certificate of Confidentiality. For most research, Certificates are obtained from NIH. If NIH funds the research project, the investigator may apply through the funding Institute. However, even if the research is not supported with NIH funding, the investigator may apply for a Certificate through the NIH Institute or Center (IC) funding research in a scientific area similar to the project.

If the research is conducting a sensitive research project that is covered by the AHRQ confidentiality statute (42 U.S.C. section299a-1(c) entitled “limitation on use of certain information”) or the Department of Justice confidentiality statute (42USC section 3789g), then a CoC is not required.

If there is an Investigational New Drug Application (IND) or an Investigational Drug Exemption (IDE), the sponsor can request a CoC from the FDA.

For more information, see the NIH Certificates of Confidentiality Kiosk (http://grants.nih.gov/grants/policy/coc/index.htm).

16.2 Mandatory Reporting

While any person may make a report if they have reasonable cause to believe that a child or elder was abused or neglected, New Jersey law mandates that certain persons who suspect child or elder abuse or neglect report this to the appropriate state agencies.

Rutgers policy requires the solicitation of informed consent from all adult research subjects and assent from children involved as research subjects, in addition to the consent of their parents. In situations where conditions of abuse or neglect might be revealed, mandated reporters should make themselves known as such to parents of children under age 18, to subjects who are children, and to subjects who are potential victims of abuse or neglect.

Investigators should consult applicable sources to determine if potential subjects should be advised of mandatory reporting requirements during the informed consent process.

16.3 Rutgers Students and Employees as Subjects

When Rutgers students and/or employees are being recruited as potential subjects, researchers must ensure that there are additional safeguards for these subjects. The voluntary nature of their participation must be primary and without undue influence on their decision. Researchers must emphasize to subjects that neither their academic status or grades, or their employment, will be affected by their participation decision.

To minimize coercion, investigators should avoid, whenever possible, the use of their students and employees in procedures which are neither therapeutic nor diagnostic. In these latter situations, investigators should solicit subjects through means such as bulletin board notices, flyers, advertisements in newspapers, and announcements in classes or laboratories other than their own..

16.4 Genetic Studies

Genetic research studies may create special risks to human subjects and their relatives. These involve medical, psychosocial, and economic risks, such as the possible loss of privacy, insurability, and employability, change in immigration status and limits on education options, and may create a social stigma. Knowledge of one's genetic make-up may also affect one's knowledge of the disease risk status of family members.

In studies involving genetic testing, several questions need to be addressed, including:

1. Will test results be given?
2. Will disease risk be quantified, including the limits on certainty of the testing?
3. Will a change in a family relationship be disclosed, such as mistaken paternity?
4. Does the subject or family member have the option not to know the results? How will this decision be recorded?
5. Could other clinically relevant information be uncovered by the study? How will disclosure of this added information occur?
6. Do any practical limitations exist on the subject's right to withdraw from the research, withdraw data, and/or withdraw DNA?
7. Is the subject permitted to participate in the study while refusing to have genetic testing (such as in a treatment study with a genetic testing component)?

For DNA banking studies, several questions need to be addressed, including:

1. Will DNA be stored or shared? If shared, will the subject's identity be known by the new recipient investigator?
2. Will the subject be contacted in the future by the investigator to obtain updated clinical information?
3. How can the subject opt out of any distribution or subsequent use of his/her genetic material?

16.5 Research Involving Coded Private Information or Biological Specimens

Rutgers policy is based on the OHRP guidance document entitled, **"Guidance on Research Involving Coded Private Information or Biological Specimens"** (August 10, 2004 http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf). This document:

1. Provides guidance as to when research involving coded private information or specimens is or is not research involving human subjects, as defined under HHS regulations for the protection of human research subjects (45 CFR part 46).
2. Reaffirms OHRP policy that, under certain limited conditions, research involving **only** coded private information or specimens is not human subjects research.

3. Provides guidance on who should determine whether human subjects are involved in research.

For purposes of this policy, *coded* means that: (1) identifying information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof (i.e., the code); and (2) a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

Under the definition of human subject in Section 2 of this policy, *obtaining* identifiable private information or identifiable specimens for research purposes constitutes human subjects research. *Obtaining* means receiving or accessing identifiable private information or identifiable specimens for research purposes. This includes an investigator's use, study, or analysis for research purposes of identifiable private information or identifiable specimens already in the possession of the investigator.

In general, private information or specimens are considered to be individually identifiable when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. Private information or specimens are not considered to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.

Research involving **only** coded private information or specimens do **not** involve human subjects 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 key to decipher the code is destroyed before the research begins;
    b. 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 that the HHS regulations do not require the IRB to review and approve this agreement); data use agreement
    c. 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
    d. there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

In some cases an investigator who obtains coded private information or specimens about living individuals under one of the conditions cited in 2(a)-(d) above may (1)

unexpectedly learn the identity of one or more living individuals, or (2) for previously unforeseen reasons now believe that it is important to identify the individual(s). If, as a result, the investigator knows, or may be able to readily ascertain, the identity of the individuals to whom the previously obtained private information or specimens pertain, then the research activity now would involve human subjects. Unless this human subjects research is determined to be exempt (See Section 7.3), IRB review of the research would be required. Informed consent of the subjects also would be required unless the IRB approved a waiver of informed consent (See Section 9.3).

16.5.1 Who Should Determine Whether Coded Private Information or Specimens Constitutes Human Subjects Research

The investigator submits a formal submission, the request must include sufficient documentation of the activity to support the determination.

16.6 International Research

The IRB will review all international research utilizing human participants to assure adequate provisions are in place to protect the rights and welfare of the participants.

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 Rutgers 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, Rutgers 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 Rutgers 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 Rutgers researchers with knowledge of the region, or other experts on the region. These individuals may either provide a written review of a particular protocol or attend an IRB meeting to provide the Rutgers 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.

16.6.1 Responsibilities

1. It is the responsibility of Rutgers' 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 Rutgers' investigator and the foreign institution or site to confirm the qualifications of the researchers and research staff for conducting research in that country(ies).
3. It is the responsibility of Rutgers' investigator and the foreign institution or site to ensure that the following activities will occur.
    a. Initial review, continuing review, and review of modification
    b. Post-approval monitoring
    c. Handling of complaints, non-compliance and unanticipated problems involving risk to subjects or others.

    The IRB will not rely on a local ethics committee that does not have policies and procedures for the activities listed above.
4. It is the responsibility of Rutgers' 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 participants, etc.).

16.6.2 Consent Documents

The informed consent documents must be in a language understandable to the proposed participants. Therefore, the IRB will review the document and a back translation of the exact content contained in the foreign language informed consent document which must be provided by the Investigator, with the credentials of the translator detailed in the IRB application or amendment form. Verification of the back translation should be made available for the IRB file.

16.6.3 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, there is a plan for coordination and communication with the local IRB/IECs.

The IRB will require documentation of regular correspondence between Rutgers' investigator and the foreign institution or site and may require verification from sources other than Rutgers' investigator that there have been no substantial changes in the research since its last review.