

**ROWAN UNIVERSITY  
COMMITTEE FOR THE PROTECTION OF  
HUMAN SUBJECTS**

**INSTITUTIONAL REVIEW BOARD (IRB)  
GUIDELINES FOR  
BIOMEDICAL, BEHAVIORAL, EDUCATIONAL  
AND SOCIAL SCIENCES RESEARCH**

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GUIDELINES FOR  
BIOMEDICAL, BEHAVIORAL, EDUCATIONAL AND SOCIAL SCIENCES RESEARCH  
INVOLVING HUMAN SUBJECTS**

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**APPENDIX**

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## **BIOMEDICAL & BEHAVIORAL RESEARCH INVOLVING HUMAN SUBJECTS**

### **INTRODUCTION**

Scientific inquiry, scholarly contributions, creativity, and academic accomplishment can take many forms and may vary among disciplines. All faculty members at Rowan University (Full-time and Adjunct Faculty), students and staff are ultimately responsible for the scholarly character, accuracy, reliability of their own research, safeguarding of research subjects and the research environment in which they work pursuant to Federal regulations, state regulations, university policies, funding agency requirements, and contractual commitments.

Rowan University referred to as “Institution”, has always considered research involving human subjects paramount to our research enterprise. Therefore, the Institution has embraced protecting the rights and welfare of research subjects by providing assurance to the Office for Human Research Protections (OHRP) to comply with federal regulations [Title **45 CFR 46** (Common Rule) and Title **21 CFR 50 and 56** (FDA)] for all human subjects research conducted regardless of the funding source. This includes all research involving human subjects under the direction of any employee or agent in connection with his/her institutional responsibilities or use of university’s academic or non-academic titles. Noncompliance with this assurance means losing eligibility for all federal and other forms of sponsored funding. Additionally, it may cause financial and reputational damage to our institution.

Protecting human subjects in research is a collaborative effort that demands the vigilance of Institution’s administration faculty, staff, and students in partnership with the local community, state and federal agencies. The primary objective of this guidance is to fully inform investigators of the complexity of ethical and compliance issues with the understanding that a well-informed investigator will effectively utilize the manual early in the protocol development process. The manual is updated as often as necessary; however, not less than once in two years.

The mission of Human Subject Protection Program (HSPP) at the Institution is to:

- Safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are protected
- Provide timely and high quality education, review and monitoring of human research projects
- Assist investigators in designing a research study that embraces ethical and responsible conduct of human subject research
- Facilitate excellence in human subjects research
- Establish a formal process to monitor, evaluate and continually improve the protection of human research participants
- Provide sufficient resources for the program
- Implement oversight of research protection

- When appropriate, intervene in research and respond directly to concerns of research participants
- Implement the research protocol strictly adhering to the policies described in this guidelines document and
- Engage human research volunteer participants through proper informed consent process.

The Institution owes our research subjects nothing less.

## ARTICLE 1 - GENERAL PRINCIPLES

### 1.1 Statement of Policy and Authority

As provided in the Institution's Federal Wide Assurance (FWA) of compliance with the Department of Health and Human Services (DHHS) Regulations for Protection of Human Research Subjects, **FWA 00007111, IORG0003575** (the "Assurance"), Rowan University (hereinafter "Institution ") acknowledge and accept its responsibility as described in the "Belmont Report" (**Appendix 1**) to protect the rights and welfare of human subjects in research investigations. The Committees for the Protection of Human Subjects are the committees formally designated by the Institution as its Institutional Review Board ("IRB") to review, approve initiation of, and conduct continuing review of biomedical, social and behavioral research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of human subjects by determining that the research proposals are in compliance with:

- A. General academic standards for advancing and disseminating scientific knowledge.
- B. Identifiable social and community interests.
- C. Institutional objectives of advancing social and behavioral sciences, diagnosis, prevention, control, and treatment of disease in humans.
- D. Applicable Food and Drug Administration (FDA) (**Appendix 2**), Common Rule (**Appendix 3**), and other applicable regulations.
- E. Projects directly involving and/or individually identifiable human subjects shall conform to the scientific, legal, and ethical principles which guide all research and shall emerge from a sound theoretical basis and follow accepted research design.

Institution's Human Subject Protection Program (HSPP) operates under the authority of the Institution's policy "Human Subjects Research: Protection of Human Subjects" adopted on July 1, 2013 (**Appendix 4**). As stated in that policy, the operating procedures in this document "serve as the governing procedures for the conduct and review of all human research conducted under the auspices of the HSPP."

Institution's Guidelines for Human Research Protection detailed below provide the guidelines and regulations governing research with human subjects and the requirements for submitting research proposals for review by Institution's IRBs. The policies and procedures are updated periodically or whenever a change is required due to regulatory changes and university policies but not less than once in two years and revised by the IRB Director, and the Institutional Review Board. The Institution's Vice President for Research or his/her designee will review and approve the policies and procedures.

The IRB Director 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 the Institution's website <https://sites.rowan.edu/officeofresearch/compliance/irb/index.html>, as well as <https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/index.html>, 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 or IRB website announcements.

The human subject protection program 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 (IO), the IRB Director, the campus IRBs, other committees or subcommittees addressing human subjects protection (e.g., Biosafety, Radiation Safety, Radioactive Drug Research, Conflict of Interest and Research Integrity), investigators, IRB staff, research staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer). 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 roles and responsibilities of members in this comprehensive program are clearly described in these guidelines.

The IO, Vice President for Research and IRB Director will review the activity of the campus IRBs on at least on an annual basis and make a determination as to the appropriate number of IRBs that are needed for the institution. This determination will be based on the evaluation of the performance of IRB as described in Section 2.8. The performance of the non-Rowan IRBs will also be evaluated on an annual basis.

## **1.2 Engagement**

In general, the Institution is considered engaged (including non-government funded research activity) when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) individually identifiable private information and identifiable biospecimens or (3) the informed consent of human subjects for the research. The following two sections apply these concepts for Institution being engaged or not.

The institution is considered engaged in an HHS-conducted or -supported non-exempt human subjects research project when the involvement of Institution's employees or agents in that project includes any of the following: <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-engagement-of-institutions/index.html>):

- A. When the Institution receives an award through a grant, contract, or cooperative agreement directly from HHS for the non-exempt human subjects research (i.e. awardee institutions), even where all activities involving human subjects are carried out by employees or agents of another institution.
- B. When Institution's employees or agents intervene for research purposes with any human subjects of the research by performing invasive or noninvasive procedures. Examples of invasive or noninvasive procedures include drawing blood; collecting buccal mucosa cells using a cotton swab; administering individual or group counseling or psychotherapy; administering drugs or other treatments; surgically implanting medical devices; utilizing physical sensors; and utilizing other measurement procedures.
- C. When Institution's employees or agents intervene for research purposes with any human subject of the research by manipulating the environment. Examples of manipulating the environment include controlling environmental light, sound, or temperature; presenting sensory stimuli; and orchestrating environmental events or social interactions.
- D. When Institution's employees or agents interact for research purposes with any human subject of the research. Examples of interactions include engaging in the protocol-derived communication or interpersonal contact; asking someone to provide a specimen by voiding or spitting into a specimen container; and conducting research interviews or administering questionnaires.
- E. When Institution's employees or agents obtain the informed consent of human subjects for the research.
- F. When Institution's employees or agents obtain for research purposes identifiable private information or identifiable biological specimens from any source for the research. It is important to note that, in general, Institution's employees or agents obtain identifiable private information or identifiable specimens for non-exempt human subject's research are considered engaged in the research, even if the institution's employees or agents do not directly interact or intervene with human subjects. In general, obtaining identifiable private information or identifiable specimens includes, but is not limited to:
  - a. Observing or recording private behavior;
  - b. Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided by another institution; and
  - c. Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.

In general, OHRP (Office for Human Research Protections) considers private information or specimens to be individually identifiable as defined in 45 CFR 46.102(f) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems.



### 1.3 Non-Engagement

The Institution is not considered engaged in an HHS-conducted or -supported non-exempt human subjects research project if the involvement of Institution's employees or agents in that project is limited to one or more of the following.

The following are scenarios describing the types of institutional involvement that would make an institution not engaged in human subjects' research; there may be additional such scenarios:

- A. When Institution's employees or agents perform commercial or other services for investigators provided that all of the following conditions also are met:
  - a. The services performed do not merit professional recognition or publication privileges;
  - b. The services performed are typically performed by those institutions for non-research purposes; and
  - c. The institution's employees or agents do not administer any study intervention being tested or evaluated under the protocol.

The following are some examples, assuming the services described would not merit professional recognition or publication privileges:

- a. An appropriately qualified laboratory whose employees perform; routine serum chemistry analyses of blood samples for investigators as a commercial service;
  - b. A transcription company whose employees transcribe research study interviews as a commercial service;
  - c. Hospital whose employees obtain blood through a blood draw or collect urine and provide such specimens to investigators as a service and
  - d. A radiology clinic whose employees perform chest x-rays and send the results to investigators as a service.
- B. When the Institution (including clinics and private practices) is not selected as a research site whose employees or agents provide clinical trial-related medical services that are dictated by the protocol and would typically be performed as part of routine clinical monitoring and/or follow-up of subjects enrolled at a study site by clinical trial investigators (e.g., medical history, physical examination, assessment of adverse events, blood test, chest X-ray, or CT scan) provided that all of the following conditions also are met:
    - a. the institution's employees or agents do not administer the study interventions being tested or evaluated under the protocol;
    - b. the clinical trial-related medical services are typically provided by the institution for clinical purposes;
    - c. the institution's employees or agents do not enroll subjects or obtain the informed consent of any subject for participation in the research; and

- d. when appropriate, investigators from an institution engaged in the research retain responsibility for:
  - i. Overseeing protocol-related activities; and
  - ii. Ensuring appropriate arrangements are made for reporting protocol-related data to investigators at an engaged institution, including the reporting of safety monitoring data and adverse events as required under the IRB-approved protocol.

Note: When Institution is not initially selected as research sites whose employees or agents administer the interventions being tested or evaluated in the study such as administering either of two chemotherapy regimens as part of an oncology clinical trial evaluating the safety and effectiveness of the two regimens generally would be engaged in human subjects research.

- C. When Institution (including private practices) is not initially selected as a research site whose employees or agents administer the study interventions being tested or evaluated under the protocol limited to a one-time or short-term basis (e.g., an oncologist at the institution administers chemotherapy to a research subject as part of a clinical trial because the subject unexpectedly goes out of town, or is unexpectedly hospitalized), provided that all of the following conditions also are met:
  - a. an investigator from an institution engaged in the research determines that it would be in the subject's best interest to receive the study interventions being tested or evaluated under the protocol;
  - b. the institution's employees or agents do not enroll subjects or obtain the informed consent of any subject for participation in the research;
  - c. investigators from the institution engaged in the research retain responsibility for:
    - i. overseeing protocol-related activities;
    - ii. ensuring the study interventions are administered in accordance with the IRB-approved protocol; and
    - iii. ensuring appropriate arrangements are made for reporting protocol-related data to investigators at the engaged institution, including the reporting of safety monitoring data and adverse events as required under the IRB-approved protocol; and
    - iv. An IRB designated on the engaged institution's FWA is informed that study interventions being tested or evaluated under the protocol have been administered at an institution not selected as a research site.
- D. When Institution's employees or agents:
  - a. inform prospective subjects about the availability of the research;
  - b. provide prospective subjects with information about the research (which may include a copy of the relevant informed consent document and other IRB approved materials) but do not obtain subjects' consent for the research or act as representatives of the investigators;

- c. provide prospective subjects with information about contacting investigators for information or enrollment; and/or
- d. Seek or obtain the prospective subjects' permission for investigators to contact them.

An example of this would be a clinician who provides patients with literature about a research study at another institution, including a copy of the informed consent document, and obtains permission from the patient to provide the patient's name and telephone number to investigators.

- E. When Institution (e.g., schools, nursing homes, businesses) permit use of their facilities for intervention or interaction with subjects by investigators from another institution.

Examples would be a school that permits investigators from another institution to conduct or distribute a research survey in the classroom; or a business that permits investigators from another institution to recruit research subjects or to draw a blood sample at the work site for research purposes.

- F. When Institution's employees or agents release to investigators at institution identifiable private information or identifiable biological specimens pertaining to the subjects of the research.

Note that in some cases the institution releasing identifiable private information or identifiable biological specimens may have institutional requirements that would need to be satisfied before the information or specimens may be released, and/or may need to comply with other applicable regulations or laws. In addition, if the identifiable private information or identifiable biological specimens to be released were collected for another research study covered by **45 CFR part 46**, then the institution releasing such information or specimens should:

- a. Ensure that the release would not violate the informed consent provided by the subjects to whom the information or biological specimens pertain **(under 45 CFR 46.116)**, or
- b. If informed consent was waived by the IRB, ensure that the release would be consistent with the IRB's determinations that permitted a waiver of informed consent under **45 CFR 46.116 (c) or (d)**.

Examples of institutions that might release individually identifiable private information or identifiable biological specimens to investigators at another institution include:

- a. Schools that release identifiable student test scores;
- b. An HHS agency that releases identifiable records about its beneficiaries; and
- c. Medical centers that release identifiable human biological specimens.

Note that, in general, when institution's employees or agents obtain the identifiable private information or identifiable biological specimens from the releasing institution would be engaged in human subjects' research.

- G. When Institution's employees or agents:
- a. Obtain coded private individually identifiable information or identifiable biological specimens from another institution involved in the research that retains a link to individually identifiable information (such as name or social security number); and
  - b. Are unable to readily ascertain the identity of the subjects to whom the coded information or specimens pertain because, for example:
    - i. The institution's employees or agents and the holder of the key enter into an agreement prohibiting the release of the key to those employees or agents under any circumstance;
    - ii. The releasing institution has IRB-approved written policies and operating procedures applicable to the research project that prohibit the release of the key to the institution's employees or agents under any circumstances; or
  - c. There are other legal requirements prohibiting the release of the key to the institution's employees or agents.

For purposes of this Guidance, coded means that:

- i. Individually identifiable private information (such as name or social security number) that would enable the investigator to readily ascertain the identity of the individual to whom the individually identifiable private information or individually identifiable biospecimens pertain has been replaced with a number, letter, symbol, and/or combination thereof (i.e., the code); and
- ii. A key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

Although this scenario resembles some of the language in OHRP's Guidance on Research Involving Coded Private Information or Biological Specimens, it is important to note that OHRP's Guidance on Research Involving Coded Private Information or Biological Specimens addresses when research involving coded private information or specimens is or is not research involving human subjects, as defined in **45 CFR 46.102(f)** (see

<http://www.dhhs.gov/ohrp/policy/cdebiol.pdf>). As stated above, this Guidance on Engagement of Institutions in Human Subjects Research is only applied to research projects that have been determined to involve human subjects and that are not exempt under HHS regulations at **45 CFR 46.101(b)**.

8. When Institution's employees or agents access or utilize individually identifiable private information only while visiting an institution that is engaged in the research, provided their research activities are overseen by the IRB of the institution that is engaged in the research.
9. When Institution's employees or agents access or review identifiable private information for purposes of study auditing (e.g. a government agency or private company will have access to individually identifiable study data for auditing purposes).

10. When Institution's employees or agents receive identifiable private information for purposes of satisfying U.S. Food and Drug Administration reporting requirements.
11. When Institution's employees or agents author a paper, journal article, or presentation describing a human subjects research study.

#### **1.4 Principles**

Human subject research conducted at the Institution is guided by the ethical principles set forth in "Ethical Principles and Guidelines for the Protection of Human Subjects of Research referred to as *The Belmont Report*." (**Appendix 1**). The actions of Institution will also conform to all applicable federal, state, and local laws, regulations and institutional policies.

The Institution further recognizes that research with human subjects raises unavoidable ethical dilemmas because the participants in research undergo risks sometimes to benefit others through the acquisition of new knowledge. Even in clinical trials that test new therapies for the participant's medical condition, the prospect of benefit is uncertain, and there may be unanticipated risks. Thus, the Institution aims to balance the benefits of research for improving the well-being of research subjects and clinical care with the protection of research participants from inappropriate risks. Independent review of research studies and informed consent by participants are the two fundamental protections federally mandated by the Common Rule for participants in human research. Therefore, the Institution asserts that the protection of participants in research is grounded in basic civil and human rights. The Institution intends to continue to develop guidelines that allow valuable research to proceed, while adequately protecting research participants and to maintain public trust in research and prevent harm to participants.

The mechanisms by which the rights, welfare, safety are being protected include:

- A. A formal process to review, approve and monitor human subject research.
- B. Provide sufficient resources for the program to flourish.
- C. Educate and train investigators about their responsibility on the ethical and responsible conduct of research.
- D. Improve the quality of research by identifying errors that might occur during the implementation of a protocol and take appropriate corrective measures.
- E. Be attentive to research participant's concerns and properly respond to their concerns.

#### **1.5 IRB Authority Jurisdiction**

IRBs at the Institution are charged with reviewing responsibilities of research conducted by faculty, students and staff at the Glassboro campus, at Rowan University Osteopathic School of Medicine (RowanSOM), social and behavioral research performed at Cooper

Medical School of Rowan University and researchers using data from New Jersey Department of Health (NJDOH), repositories. Any collaborative research conducted by Rowan University faculty, students and staff at another institution. The authority also includes research conducted by non-Institution's employees who use Rowan University as a research site.

### **1.5.1 Authority**

- A. To approve, require modifications in (to secure approval), or disapprove all research activities overseen and conducted under the auspices of the Institution;
- B. To conduct IRB review and approve benign behavioral intervention studies information in conjunction with the collection of information;
- C. To review and approve use or storage of identifiable private identifiable biospecimens using a boilerplate consent;
- D. 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. Suspensions shall include a statement of the reasons for the IRB's action to suspend an ongoing activity. Suspensions will be reported promptly to the investigator, appropriate institutional officials such as the department head, vice president of research, and dean of investigator's college or school, and the department or agency head, if federally funded or to the foundations that funded research;
- E. To observe, or have a third party observe, the consent process when required by IRB an
- F. To observe, or have a third party observe, the conduct of the research.

Human subject 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. Institution's 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.

### **1.5.2 Jurisdictions**

- A. All clinical trials sponsored by pharmaceutical companies (drugs, biologics and devices) and oncology studies will be referred to the Western/Copernicus Institutional Review Board (WIRB) for review and approval.
- B. Approvals to begin a clinical trial will come from the Western/Copernicus Institutional Review Board (WIRB).
- C. All internally-initiated clinical studies conducted by Institution's, faculty, staff and students with or without protected health information are reviewed by Institution's IRBs.

- D. Social and behavioral studies may be approved by any of the Institution's IRBs. All studies containing protected health are reviewed by IRB#2 at Stratford.
- E. Institution's IRBs can sign an authorization agreement (<http://www.hhs.gov/ohrp/assurances/forms/irbauthorizpdf.pdf>) with another IRB for review on a need basis. For single IRB review of multisite studies the IRB offices at the Institution will ensure such sites have an FWA for federally funded studies. Principal IRB conducting a multisite research will take into account local context provided by the Institution.
- F. Research that has been reviewed and approved by the IRB may be subject to review and disapproval by the officials of the institution. However, these officials do not have the authority to approve a study that has been disapproved by the IRB.

## **1.6 Questions, Complaints or Concerns of Research Subjects**

### **1.6.1 Questions, Concerns about a Study**

The Consent form that subjects receive when they are invited to be research subjects includes contact information if they have questions or concerns about the study.

### **1.6.2 Rights of a Research Subject**

Subjects may call the investigator, study doctor or the IRB offices to discuss any questions about the study and their rights. Investigators and study doctors names and contact information is on the consent form. At the time of consenting, investigators and study doctors explain the study and patient's rights to participate in the study and inform the subject how to reach out to the investigator or study doctor using the contact information provided on the consent form. The consent form also provides contact information to talk to someone in the IRB office. Strict confidentiality will be maintained when subjects like to discuss their rights in private.

### **1.6.3 Anonymous Questions/Complaints by Research Subjects**

If research subjects have concerns or complaints about the research or research staff and you do not wish to give their name, they may call toll free hotline at 1-855-431-9967. This is a 24 hour hotline.

### **1.6.4 Anonymous Questions/Complaints by Researchers**

The Human Subjects Protection Program Office at Rowan University and the Institutional Review Boards (IRB) want to meet their primary responsibility of protecting human subjects who participate in research at the University. They also want to work in a cooperative and collegial manner with investigators at the University to assure this protection as a team. Unfortunately, sometimes the best of intent does not always yield the best of results. If researchers have concerns or complaints about the service they received from the IRB Office or one of the IRBs, they have been unable to resolve the problem, they must

contact the Director of Research Compliance using the following contact information.

Eric Gregory

Phone: 856-256-4058

Email: [gregorye@rowan.edu](mailto:gregorye@rowan.edu)

Or, if the matter is still not resolved contact:

Vice President for Research, Mei Wei Ph.D., at:

Phone: 856-256-4090

Email: [weim@rowan.edu](mailto:weim@rowan.edu).

If research subjects have concerns or complaints about the research or research staff and you do not wish to give their name, they may call toll free hotline at 1-855-431-9967. This is a 24 hour hotline.

### **1.7 Relationship Among Institution's IRB Components**

All IRBs under the Institution's Federalwide Assurance (**Appendix 5**) function independently except in certain circumstances when the Chair of one of the IRBs may request that a study scheduled for review or continuing review at one of the Institution's IRBs can be referred for review to another Institution's IRB (internal) listed in the assurance document. In order to meet this exception, the reviewing IRB is properly constituted ensuring expertise and membership requirements to approve a study. This generally occurs when social and behavioral studies originating from the main campus are the object of review. Clinical trials involving drugs, biologicals and devices are reviewed by RowanSOM IRB.

### **1.8 Studies Requiring IRB Review**

To assure the protection of human subjects and to comply with Federal regulations [Common Rule (**45 CFR 46**) and FDA (**21 CFR Part 51 and 56**) regulations and, the Institution requires IRB review and approval whenever biomedical or social and behavioral research projects are undertaken by the Institution's faculty, staff, employees, agents, students, or New Jersey Department of Health (NJDOH) researchers and other researchers who request and use data from NJDOH repositories, which, in whole or in part, involve human subjects or identifiable private information and identifiable bio-specimens material.

In general systematic investigations include:

- A. Clinical trials;
- B. Surveys and questionnaires;
- C. Interviews and focus groups;
- D. Analyses of existing data;
- E. Existing and prospectively collected biological specimens;
- F. Epidemiologic studies;
- G. Evaluation of social or educational programs;
- H. Cognitive and perceptual experiments;
- I. Medical and other clinical or non-clinical chart reviews and



J. Medical and behavioral interventions (diagnosis and treatment).

Investigations designed to develop or contribute to generalizable knowledge are those designed to draw general conclusions, inform policy, or generalize findings beyond a single individual or an internal program (e.g., publications or presentations). However, research results do not have to be published or presented to qualify the experiment or data gathering as research. The intent to contribute to "generalizable (scholarly) knowledge" makes an experiment or data collection research, regardless of publication.

Research that never is published is still research. Participants in research studies deserve protection whether or not the research is published.

### 1.9 Studies not Requiring IRB Review

Studies not requiring IRB review activities are those associated with providing timely, situational awareness and priority setting during the course of an event or crisis that threatens public health including natural and man-made disasters. **Even when IRB review is not required, researchers and staff are still required to submit an e-IRB application requesting for non-human subject research determination**

**([https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/nonhumanresearch.html#p7EPMc1\\_12](https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/nonhumanresearch.html#p7EPMc1_12) ).**

The Office for Human Research Protections (OHRP) announced in the November 19, 2018 issue of the Federal Register the availability of a draft guidance document that relates to three burden-reducing provisions in the revised Common Rule that institutions may choose to implement during the delay period (July 19, 2018 through January 20, 2019) for general compliance with the revised Common Rule. The draft guidance document is titled: "Activities Deemed Not to Be Research: Public Health Surveillance, 2018 Requirements. (<https://www.hhs.gov/ohrp/draft-guidance-public-health-surveillance-activities.html>)." This guidance is still in the draft form. Hence, the following items A- I will be used to determine whether the proposed research activity constitutes non-human subject research.

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

- timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
- C. Collection and analysis of information, biospecimens, or record by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
  - D. Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense or other national security missions.
  - E. Private information or biospecimen not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems if the following conditions are both met:
    - a. the private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and
    - b. the investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
      - i. 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);
      - ii. 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
      - iii. There are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.
  - F. Certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal (**45 CFR 46.118**). These applications need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived under **45 CFR 46.101 (b) or (i)**, no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in this policy, and certification submitted, by the institution, to the department or agency.
  - G. If the proposed studies involve a group of individuals who are consultants and have been chosen for their expertise to improve the research design, such consultations **are** considered non-human subjects research.
  - H. If the studies involve a group of individuals who are brought in to test a new product (e.g. software, equipment, surveys) to identify “bugs” or problems, the research considered **non**-human subjects research because the data collected is about the product and not about the individuals. This is a Beta -Test of the product. However, if the studies involve a group of the eventual target population

who is brought in to “pilot test” a new product or intervention before researchers finalize the design of the product or intervention, the research MAY BE considered human subjects research. Pilot tests involve living individuals if the PI conducting research obtains data or individually identifiable private information.

- I. Investigator making use of certain data such as Public Use Data (publicly available) and de-identified data **Not Derived From Other Research Projects**.

Whenever a study is determined by the researcher as non-human subject research (NHSR) or study not requiring an IRB review, in such cases, the investigator **is required to submit an CIRB application in which the investigator will check the box labelled as “Non-Human Subject Research”**.

When non-human subject research (NHSR) is requested by the investigator, OHRP recommends that institutions adopt clear procedures under which the IRB (or some authority other than the investigator) determines whether proposed research is exempt from the human subjects regulations [see 45 CFR 46.101(b)]. Documentation should include the specific category justifying the exemption. (<http://www.hhs.gov/ohrp/polciy/irbgd107.html>). In such cases the nonhuman subject CIRB application will be reviewed by the IRB Director or IRB Chair or IRB member who will make a determination whether the proposed non-human subject research study qualifies as NHSR using a Non-Human Subject Reviewer Checklist in the CIRB (See Guidance Article 1.15 below). In such cases, a determination letter which states that “The activities described in this application does not meet the regulatory definition of human subjects research provided in §45 CFR 46.102 (I). Therefore, this project does not require approval by the IRB as submitted. Please note that changes to the project must be submitted to the IRB for review prior to implementation to determine if the changes incorporate elements of human subjects research activities which require IRB oversight” will be sent to the investigator.

Above listed IRB review requirements (Articles 1.7 and 1.8) applies to all such research regardless of the funding source and location of the study if it meets any of the following:

- A. The research is sponsored by the Institution.
- B. The research is conducted by or under the direction of any of the Institution's employees or agents in connection with his or her institutional responsibilities.
- C. The research is conducted using any of the Institution's property or facilities,
- D. The research involves the use of the Institution's non-public information to identify or contact human research subjects or prospective subjects.

### **1.10 Definition of Human Subjects and Research**

- A. Human subject means a living individual about whom an investigator (whether professional or student) conducting research:
  - a. Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

- b. Obtains, uses, studies, analyzes or generates identifiable private information or identifiable biospecimens.
- B. Research means a systematic investigation including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example some demonstration and service programs may include research activities. Research that does not require IRB review is described in Section 1.8 above.

### 1.11 Other Definitions

- A. Clinical trial means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.
- B. Institution means any public or private entity, or department or agency (including federal, state, and other agencies).
- C. Intervention means both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- D. Interaction means communication or interpersonal contact between investigator and subject.
- E. Identifiable private information means private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
- F. An identifiable biospecimen means a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.
- G. IRB means an institutional review board established in accordance with and for the purposes expressed in this policy.
- H. IRB approval means the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and federal requirements.
- I. Legally authorized representative means an individual or judicial other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.
- J. Minimal risk means that the probability and the 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.

- K. Private information means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).
- L. Protocol/study means the formal design or plan of an experiment or research activity or, specifically, the plan submitted to an IRB for review and to an agency for support of the research. The protocol/study includes a description of the research design and methods to be employed, the eligibility requirements for subjects and controls, the treatment regimen(s), evaluation of expected or unexpected problems, risks, and discomforts to study subjects, and the methods of analysis to be performed on the collected data.
- M. Public health authority means an agency or authority of the United States, a state, a territory, a political subdivision of a state or territory, an Indian tribe, or a foreign government, or a person or public agency, including the employees or agents of such public agency or its contractors or persons or entities to whom it has granted authority, that is responsible for public health matters as part of its official mandate.

### **1.12 List of Research Activities Considered as Human Research**

For the purpose of this manual, “research” shall include:

- A. Clinical research or study;
- B. Clinical trial;
- C. Investigator-initiated Clinical investigation;
- D. Social, educational and behavioral research through interaction, intervention, experimentation or observation;
- E. Studies involving an “investigational device” that is the object of research investigation or evaluation, but not clinical use;
- F. Studies involving an “investigational new drug” (IND) either new or “off-label” use of a drug;
- G. Studies involving “biological products” in an “investigational study”;
- H. Studies involving use of a new diagnostic method or article;
- I. Studies involving use of a new treatment modality, surgical procedure, or psychological measure in a “clinical investigation or study”;
- J. Epidemiologic studies;
- K. Existing or prospective chart reviews or records;
- L. Data mining from electronic records;
- M. Surveys and
- N. Some quality improvement activities.

### **1.13 Use of Coded Biospecimens**

Secondary research involving non-identifiable biospecimens or coded biospecimens can conduct research with such specimens without consent provided the following conditions are met:

- A. The non-identifiable biospecimens or coded biospecimens were not collected specifically for the currently proposed research project;
- B. The investigator(s) cannot readily ascertain the identity of the individual(s) to whom the non-identifiable biospecimens or coded biospecimens pertain because, for example:
  - a. The investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (note that the HHS regulations do not require the IRB to review and approve this agreement);
  - b. There are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or (c) there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.
  - c. There are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.
- C. IRB reserves the right to determine whether secondary uses of biospecimens are compatible with the original consent; this could involve consultation with the IRB that approved the original research, or review by some other body designated for this purposes. Coding will not be used to circumvent the original terms of the consent. This requirement may apply even if the original project is over and the secondary use is no longer considered to be research involving human subjects.

#### **1.14 Definition of non-human subject research for quality improvement activities (QIA)**

When quality improvement activities (QIA) are not done for research purposes, they may **not** be considered as human subject research. Examples:

- A. Implementing a practice to improve the quality of patient care or administrative performance
- B. Collecting patient or provider data regarding the implementation of the practice for clinical, practical, or administrative purposes delivering healthcare or academic activities.

#### **1.15 QIA Projects considered as human subject research**

(<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/quality-improvement-activities/index.html>.)

- A. Activities such as measuring and reporting provider performance data for clinical, practical, or administrative uses to carry out a quality improvement project and publish the results.
- B. Data that are not individually identifiable, such as medication databases stripped of individual patient identifiers, for research purposes.
- C. Introducing an untested clinical intervention for purposes which include not only improving the quality of care but also collecting information about patient

outcomes for the purpose of establishing scientific evidence to determine how well the intervention achieves its intended results

- D. QIA projects that involves research require IRB review at full board or expedited review levels depending upon the level of risk to subjects and private information
- E. QIA projects that are research must also meet all of the HIPAA requirements when participant's protected health information is used.

For further information on Quality Improvement Activities, go to

[http://www.firstclinical.com/regdocs/doc/?db=OTH\\_OHRP\\_Quality\\_Improvement](http://www.firstclinical.com/regdocs/doc/?db=OTH_OHRP_Quality_Improvement)

### **1.16 Who will determine whether human subjects are involved in research?**

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 1.9. Since the Organization will hold them responsible if the determination is not correct, investigators are advised to complete a Determination of Non-Human Subject Application through CIRB. 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 Article 1.8 of this guidance using the Human Subjects Research Determination Checklist (**Appendix 6**). Determinations regarding activities that are either clearly or clearly not human subject's research, based on the checklist, may be made by the designated IRB staff, IRB Chair or IRB Director. Determinations regarding less clear-cut activities will be referred to the IRB Chair or IRB Director, who may make the determination or refer the matter to the IRB.

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





## ARTICLE 2 - IRB OPERATIONS

### 2.1 IRB Operations

The organizational structure for human subject protection is attached (**Appendix 7**). IRBs are operated by individuals listed in the organization chart and they are required to comply with all regulatory and ethical standards and practices. IRB operations are conducted using an electronic submission, review and approval encompassed within the CIRB. IRB records are also maintained electronically within the CIRB.

### 2.2 Institutional Official (IO)

The Institutional Officials (Signatory Official) will be appointed by the President. There is no specific term for this position.

The ultimate responsibility of the human subject protection program resides with the IO. The IO for the Institution is Vice President for Research. The IO is responsible for ensuring that the Human Research Protection Program (HSPP) functions effectively and that the institution provides the resources and support necessary to comply with all requirements applicable to research involving human subjects. The IO represents the institution named in the Federalwide Assurance (FWA).

The IO for Rowan University HSPP is Vice President for Research.

The responsibilities of IO include:

- A. Designating one or more Institutional Review Boards (IRBs) that will review research covered by the institution's FWA;
- B. Providing sufficient resources, space, and staff to support the IRB's review and record keeping duties;
- C. Providing training and educational opportunities for the IRB and investigators;
- D. "Setting the tone" by promoting an institutional culture of respect and conscience, so that the ethical conduct of human subjects research is supported at the highest levels of the organization;
- E. Ensuring effective institution-wide communication and guidance on human subjects' research;
- F. Ensuring that investigators fulfill their responsibilities;
- G. Encouraging that all staff engaged in the conduct or oversight of human subject research participate in education activities;
- H. Serving as a knowledgeable point of contact for OHRP and other federal agencies, or delegating this responsibility to another appropriate individual and
- I. Depending on the organizational structure at a given institution, other administrative arrangements may be appropriate.

The IO may delegate the performance of certain oversight and operational duties to one or more individuals. Any delegation of duty must be in writing.

### 2.2.1 IO Responsibilities

- A. Appointing IRB members. Suspending or terminating the IRB membership of any individual for whom it has been determined that he/she is not fulfilling membership responsibilities and or obligations;
- B. Appointing the IRB chair or co-chairs. Suspending or terminating the appointment of any chair or co-chair he/she is not fulfilling his/her responsibilities and or obligations;
- C. Performing periodic evaluation of the performance of the IRB chairs and co-chairs and administrative staff;
- D. Managing and administering funds. Ensuring that adequate personnel, space and other resources are allocated to the HSPP;
- E. Reviewing and signing memoranda of understanding and cooperative agreements between the institution and other organizations, including those that establish reliance on IRBs of record for collaborative research (e.g., IRB Authorization Agreements, Individual Investigator Agreements);
- F. Being the point of contact for correspondence addressing human subjects research with the OHRP, FDA and other agencies as applicable, including reports to federal agencies;
- G. Ensuring that IRB members and investigators are knowledgeable to conduct research in accordance with ethical standards and all applicable regulations;
- H. Developing and implementing an educational plan for IRB members, staff and investigators;
- I. Ensuring that IRB members and investigators are knowledgeable to conduct research in accordance with ethical standards and all applicable regulations;
- J. Performing periodic evaluation of the performance of the IRB members and administrative staff;
- K. Recruiting qualified members to include expert, non-scientific and unaffiliated representation on the IRB;
- L. Reviewing and approving Standard Operating Procedures (SOPs) for the IRB and HSPP and
- M. Overseeing daily operations of the IRB and HSPP in accordance with the SOPs.

The IO does not have the authority to delegate the following responsibilities:

- A. Signatory authority for the FWA without appointing such authority in writing to an individual;
- B. Completing recommended Assurance training for the IO;
- C. Ensuring that the IRB functions independently and that its chair or chairs and members have direct access to the IO for appeal if they experience undue influence or if they have concerns about the function of the IRB and
- D. Ensuring that adequate resources, including funds, space, and personnel are provided to support the operation of the HSPP.

The IO cannot approve research that has been disapproved or not yet approved by the IRB

### **2.3 Human Subjects Protections Administrator (HPA)**

Federal Regulations require that every FWA institution should have an HPA, even if the institution relies totally on other IRBs. The HPA will be the agent of the Institution who exercises operational responsibility, on a day-to-day basis, for its program for protecting human subjects. HPA for Rowan University is the IRB Director.

HPA's responsibilities include the following:

- A. 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 program;
- B. Advising the IO on key matters regarding research at Rowan University;
- C. Implementing the Institution's human subject protection policy;
- D. Oversight of the submission, implementation and maintenance of approved FWAs and IRB registration;
- E. Securing adequate resources for the management of the program;
- F. Assisting investigators in their efforts to carry out Institution's research mission;
- G. Developing and implementing needed improvements and ensuring follow-up of actions, as appropriate, for the purpose of managing risk in the research program;
- H. 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;
- I. Serving as the primary contact at the Institution for the Office for Human Research Protections (OHRP) of the U.S. Department of Health and Human Services and other federal regulatory agencies;
- J. Day-to-day responsibility for the operation of the HSPP office, including supervision of IRB staff;
- K. Responding to faculty, student and staff questions;
- L. Working closely with the IRB chairs and IRB coordinators on the development of policy and procedures, as well as organizing and documenting the review process and
- M. Human subjects' protection administrator may also serve as IRB Director.

### **2.4. IRB Director**

The IRB Director is also the human subject protection administrator at this Institution. IRB Director is responsible for all aspects of the 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 its review by the IRB, as well as serving as the liaison between the investigators and the IRB. The IRB 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.

## **2.5 IRB Staffing**

Each IRB shall be staffed by at least one (1) full-time administrative staff person. IRB staff is selected in consultation with IO, IRB Chairs and HPA or IRB Director as per Rowan University's Human Resources policies and procedures. IRB staff is evaluated annually according to Human Resources policies and procedures. The staff members shall assist the IRB by fulfilling all record keeping, notification, recording, preparing agenda, preparing minutes of meetings and other procedural requirements as stated herein. The staff is trained to perform all administrative duties of the IRB and will be familiar with all applicable regulations and institutional guidelines and familiar with CIRB operation system. The IRB Support Staff is also responsible for IRB record retention for seven years in accordance with State of New Jersey regulations (<https://confluence.rowan.edu/display/POLICY/Records+Retention>). The IRB Support Staff is responsible for maintaining complete IRB paper/electronic files, records of all research protocols, preparing IRB agenda, IRB minutes and IRB correspondence.

## **2.6 Sponsored Programs Administration**

The Office of Sponsored Programs staff review all research agreements with federal, foundation, or non-profit sponsors. This ensures that all terms of the award are in compliance with institutional policies. Only designated senior individuals within Sponsored Programs Administration have the authority to approve research proposals and to execute externally funded research agreements that are on behalf of the institution.

When the grant or contract agreement includes human research activities that will be conducted by investigators who are not employees or agents of the Institution, a subcontract is executed between the Institution and the collaborating institution. The subcontract includes the requirement for the collaborating institution to assure compliance with federal regulations for the protection of human subjects in research and to provide documentation of current and ongoing IRB approval by submission of an executed Form 310 (as applicable). The collaborating institution must also ensure that key personnel involved in conducting human subject research subjects are in compliance with all applicable regulations (**Common Rule, Appendix 3**), FDA regulations (**Appendix 2**) and FERPA (**Appendix 8**) for the protection of human research subjects and provide documentation of education of key personnel to the Institution. If the grant or contract includes multi-sites, the sponsored program IRB office will communicate with the IRB Office to facilitate single IRB review for a multisite study, such single IRB review will require consideration of local context and an interinstitutional agreement to rely upon an external IRB or Rowan IRB as necessary.

## **2.7 Quality Assurance/Quality Improvement and Compliance Audits**

The objective of the Organization's HSPP Quality Assurance/Quality Improvement Plan is to measure and improve human research protection effectiveness, quality, and compliance with organizational policies and procedures and applicable deferral, state,

and local laws. The Quality Assurance/Quality Improvement Plan and compliance audits will be managed and implemented by the IRB Director. The IRBs conduct routine “not for cause” audits and “for cause” audits. Not for cause audits are conducted to assess, educate and train investigators to remain in compliance with federal, state and local regulations and institution policies.

For cause audits are conducted in response to regulatory and institutional concerns. In both cases, auditors are appointed by IRBs in consultation with IRB Director. Auditors will confirm whether approved protocols are implemented as approved by the IRB by examining investigator’s research records, recruitment and consenting process, observe recruitment and consenting process and other human subject research conduct issues that are pertinent to protect human research subjects. IRB-required audits may include external collaborator’s site or institution to assess compliance with federal, state and local law and IRB policies and procedures.

Audit reports are presented to the IRB for appropriate action. The results of the quality assurance activities and compliance audits are reported to the IO, investigator and investigator’s Department Chair or Dean of specific school or college. If an audit review finds that research subjects are exposed to unexpected serious harm, IRB Director will promptly report such findings to the IO, investigator and Department Chair or Dean of specific school or college. Policy for Continuous and serious non-compliance is described in **(Appendix 9)**.

In addition, periodically IRB will determine randomly which study would require verification that study is being implemented as approved by the IRB. Such random selection may include projects that are determined to be high risk, high level of enrollment, investigator who in the past had failed to comply or the determination by the IRB of possible material changes occurring without IRB approval.

## **2.8 Compliance Review for IRBs**

Compliance audits are done when directed due to concerns raised by federal agencies, external sponsors or others. The results may impact current practices and may require additional educational activities or revisions to SOPs, and noncompliance will be reported to the IO, department head and the Dean of the respective college or school. Compliance audits of IRB include the following:

- 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 organization 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 and
- M. Other monitoring or auditing activities deemed appropriate by the IRB.

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

## **2.9 Review of Human Subjects Research Activities by Other Ancillary Committees in the Institution**

Institution's IRBs coordinate reviews with other institutional committees as described below. None of these committees are a formal part of the Institution's IRB structure, but there is communication between the committees regarding status of review and/or conditions of approval. Other institutional committees also share the responsibility for following guidelines in the collective effort to protect human subjects; however, the final authority for participation of human subjects in research falls on the IRB.

Researchers are not required to wait for the approval of the other institutional review committees before submitting a proposal to the IRB. These reviews are generally conducted in parallel when IRB is conducting its review. However, IRB's final approval will be held until documentation of approvals from other Institution's review committees and the approval is communicated to the IRB.

### **2.9.1 Radiation Safety Committee (RSC)**

The Radiation Safety Office (RSO) provides expertise with regards to accepted radiation protections regulations and practices. For human subject-related radiation safety issues, the Radiation Safety Officer for the Institution reviews and makes appropriate decisions for the level of review as described below. The Radiation Safety Officer reviews any research that involves the use of X-ray, radioisotopes, or lasers or infrared or near infrared devices. Approval by the IRB is contingent upon approval by the RSC; however, review by the two committees may occur concurrently.

The RSO is charged with ascertaining that all experimental or research uses of radioactive materials and/or ionizing radiation in or on human subjects conform to the currently accepted radiation protection regulations and practices (<http://www.state.nj.us/dep/rpp/index.htm>). The Institution's Radioactive Material License with the State of New Jersey is on file. If RSC review is completed after the IRB review, the IRB chair reviews any RSC comments. If the chair believes the suggested changes are appropriate and qualify as minor modifications, the IRB chair reviews these through an expedited process. If changes exceed minor modifications, the IRB chair refers the application back to the full board for review. If the chair determines that full-committee review is necessary, the HSPA through the ORRC will notify the investigator and the RSO that the study has been placed on administrative hold until the concerns are addressed by the IRB. The RSC also serves as the RSC for applications sent to WIRB/Copernicus.

To ensure protection for human subjects against radiation, research proposals are categorized and reviewed as follows:

- Class 1:** Radiation Exposure or application of radioactive material as related to a standard clinical procedure that the individual as a patient would have received anyway. The radiation Safety Officer (RSO) will approve such projects.
- Class 2:** Radiation exposure or application of a radioactive material due to a standard clinical procedure that the human subject would not have normally received but which is part of proposed research protocol.
- Class 3:** Radiation exposure due to a non-standard procedure

Procedure for approval is dependent on particular class under which the proposed protocol involving human use falls:

- Class 1:** No Radiation Safety Committee or Radiation Safety Office (RSO) review will be necessary.
- Class 2:** Application and associated consent form will receive a summary review jointly by the IRB and the Chair of the RSC. The Radiation Safety Office shall assure that the radiation doses are appropriately documented. Full review by the RSC will be necessary, but the action taken will be reported, for the record, at the next Radiation Safety Committee.
- Class 3:** The full IRB and the RSC must review Application and associated consent forms. There may be a separate RSO at Kennedy Memorial Hospital (KMH). In that case, one or both (Institution's RSC and/or KMH's RSC) may conduct independent reviews to approve or disapprove research protocols involving radiation. Recommendations from RSC will be forwarded to the IRB for discussion at the time of the review to ensure that subjects are protected from harm induced by radiation.

### 2.9.2 Institution Biosafety Committee (IBC)

The IBC ensures that research involving recombinant DNA complies with the National Institutes of Health (NIH) Science Policy Office. <https://osp.od.nih.gov/biotechnology/nih-guidelines/>. The IBC does not review research involving the use of recombinant DNA materials in clinical trials. Clinical trials involving recombinant DNA materials are reviewed by WIRB's IBC. Use of recombinant materials in basic research (non-human subject's bench research) that is not exempt from NIH recombinant DNA guidelines are reviewed and approved by the IBC.

### **2.9.3 Scientific Review of Cancer Trials**

The Institution does not have a special committee that reviews all cancer clinical trials. The IRB reviews all intramural studies or cooperative group studies. External Industry sponsored cancer clinical trials are sent to WIRB for review and approval.

### **2.10 Cooperative Research Projects**

- A. Cooperative research projects are those projects covered by this policy that involve more than one institution. In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy.
- B. When the institution is engaged in cooperative research it will rely upon approval by a single IRB for that portion of the research that is conducted elsewhere in the United States. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.
- C. The following research is not subject to this provision:
  - a. Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or
  - b. Research for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context.
- D. For research not subject to 2.10.B. of this section, the Institution may enter into joint review arrangement, rely on the review of another IRB, or make similar arrangements for avoiding duplication.

When the Institution relies on another IRB, the IRB Director will review the policies and procedures of the IRB providing the review to ensure that they meet Institution's standards. If the other institution holds a FWA, it will be assumed that Institution's standards are being met.

When the Institution 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 Institution's IRB or (ii) through



subsequent review by appropriate designated institutional officials, such as the Chairperson and/or other IRB members.

If the Institution's IRB 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 participating facilities (e.g. VA Research and Development Committee approval) prior to enrollment of participants.

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

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

When the Institution is engaged in only part of a cooperative research project, the Institution's IRB only needs to approve the part(s) of the research in which the investigator is engaged. For example, if the Institution is operating the statistical center for a study that receives identifiable private information from multiple other institutions,

the Institution's IRB reviews and approves the research activities related to the receipt and processing of the identifiable private information by the statistical center.

### **2.11 Cooperative agreements for FDA related research**

The Food and Drug Administration (FDA) and Department of Health and Human Services (HHS) regulations permit institutions involved in multi-institutional studies to use reasonable methods of joint or cooperative review [**21 CFR 56.114 and 45 CFR 46.114, respectively (Appendix 2 and 3)**]. While the IRB assumes responsibility for oversight and continuing review, the clinical investigator and the research site retain the responsibility for the conduct of the study.

The regulatory provision for cooperative review arrangements may be applied to different types of cooperative clinical investigations. Examples include research coordinated by cooperative oncology groups and participation by investigators and subjects in a clinical study primarily conducted at or administered by another institution. Often, one institution has the primary responsibility for the conduct of the study and the responsibility for administrative or coordinating functions. At other times, multi center trials may be coordinated by an office or organization that does not actually conduct the clinical study or have an IRB.

The cooperative research arrangements between institutions may apply to the review of one study, to certain specific categories of studies or to all studies. A single cooperative IRB may provide review for several participating institutions, but the respective responsibilities of the IRB and each institution should be agreed to in writing.

The Institution may agree to delegate the responsibility for initial and continuing review to another institution's IRB. In turn, the IRB agrees to assume responsibility for initial and continuing review. The institution when delegating the responsibility for review understands that it is agreeing to abide by the reviewing IRB's decisions. In that case, the Institution remains responsible for ensuring that the research conducted within its own institution is in full accordance with the determinations of the IRB providing the review and oversight.

If the Institution's IRB agrees to review studies conducted at another institution, then the Institution bears the responsibility for initial and continuing review of the research. In that case the Institution's IRB takes into account the required criteria for approval, the facilities and capabilities of the other institution, and the measures taken by the other institution to ensure compliance with the IRB's determinations. The reviewing IRB needs to be sensitive to factors such as community attitudes.

The agreement for IRB review of cooperative research will be documented. Depending upon the scope of the agreement, documentation may be simple, in the form of a letter, or more complex such as a formal memorandum of understanding. In the case of studies supported or conducted by HHS, arrangements or agreements may be subject to approval

by HHS through the Office for Human Research Protections (OHRP) and will be executed in accordance with OHRP's instructions. Whatever form of documentation is used, copies will be furnished to all parties to the agreement, and to those responsible for ensuring compliance with the regulations and the IRB's determinations. The IRB's records will include documentation of such agreements.

When an IRB approves a study, it notifies (in writing) the clinical investigator and the institution at each location for which the IRB has assumed responsibility [**21 CFR 56.109(d)**]. All required reports from the clinical investigators will be sent directly to the responsible IRB with copies to the investigator's institution, as appropriate.

Another form of cooperative research activity is a multi-institutional IRB that oversees the research activities of more than one institution in a defined area, such as a city or county. Such an IRB will be formed by separate but cooperating institutions and eliminates the need for each facility to organize and staff its own IRB. A variation of this is an IRB that is established by a corporate entity to oversee research at its operating components, for example, a hospital system with facilities at several locations.

## **ARTICLE 3. IRBs, IRB CHAIRS AND MEMBERSHIP**

### **3.1 IRBs, IRB Chairs and Membership**

The Institution has established two Institutional Review Boards (IRBs) to ensure the protection of human subjects in human subjects research conducted under the auspices of the Organization. The Institution has authorized two IRBs to fulfill this function. All Institution's IRBs apply appropriate policies and procedures described in this guidance manual. In addition, the Institution utilizes an external IRB for the purpose of reviewing clinical trials sponsored by the Industry.

- Western IRB (WIRB-Copernicus Group): the WIRB option is available to Institution's clinical investigators who conduct industry-initiated, industry-sponsored research activities in which all activities are conducted at Institution's sites and by Institution's personnel.

The external IRB listed above serves as the IRB-of-record for the Institution and has the same authority as the Institution's IRBs and all determinations and findings of the external IRBs are equally binding on all research under the auspices of the Institution.

Policies and Procedures for submitting protocols to WIRB are posted at:

<https://sites.rowan.edu/officeofresearch/compliance/irb/westernirb/index.html>.

According to this policy, all new initial applications must be submitted electronically through CIRB. Investigators must make sure WIRB is selected as the IRB of record.

Upon receipt by WIRB, WIRB will issue a tracking number to the investigator and the research coordinator so they may track the application status. After WIRB determines the status of approval/disapproval, the WIRB will communicate the decision to investigator and the research coordinator. WIRB will also contact the investigator and the research coordinator about any issues that arose at the review process, and about those matters relevant to the conduct of the study. WIRB will arrange for monitoring ongoing research, as its policies and procedures require. Copies of approval of modifications to a trial must be uploaded to CIRB. In addition, the WIRB will communicate its determination to the IRB Office at Rowan University SOM.

### **3.2 IRB Chairs**

The IO in consultation with the IRB Director or HPA, university academic leadership and IRB members appoints IRB Chairs. The criteria for selection are based on the institution's research goals and objectives and human subject research experience. The IRB Chair should be a highly respected individual, from within the Institution fully capable of managing the IRB, and the matters brought before it with fairness, impartiality and avoiding conflict of interest.

The responsibility 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 the IRB Director.

The IRB Chair advises the IO, the HPA or the IRB Director about IRB member performance and competence.

The performance of IRB Chair will be reviewed on an annual basis by the IO 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 may be removed.

The chairs of the IRB shall serve a term of three (3) years. IRB chairs who have served three (3) year terms may be reappointed at the discretion of the IO in consultation with the IRB Director. Federal regulations require that the IRB Chairs complete the CITI IRB training for Chairs and web-based OHRP modules to ensure that the Chairs are aware of their responsibilities under the FWA.

### **3.3 IRB Vice-Chairs**

IRB vice chairs may be appointed by IO in consultation with the IRB Chair, and the IRB Director. Vice chairperson will have the same qualifications of the IRB Chairperson. The Vice Chair will fulfill all of the responsibilities of the chair when chair is not available or when the chair is conflicted with the review process. Vice-chairs shall serve a term of three (3) years. The vice-chair will chair IRB meetings in the absence of the Chair or when the Chair has a conflicting interest with a research protocol or a matter in front of the IRB. In the event that Chair and Vice Chair have a conflict, a senior member of the IRB may chair the meeting. Vice-chairs will have at least one year of experience serving as a member of any IRB. IRB vice-chairs who have served three (3) year terms may be reappointed at the discretion of IO and the IRB Director. Vice Chairs may be appointed for additional terms.

### **3.4 IRB Members**

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. The structure and composition of the IRB must be appropriate to the amount and nature of the research that is reviewed. Every effort is made to have member representation that has an understanding of the areas of specialty that encompasses most

of the research performed at the Institution. Individuals from the Institution's Administrative offices and affiliate institutions such as the IO and legal counsel 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 Institution has established procedures (See Article 4) that specifically outline the requirements of protocol review by individuals with appropriate scientific or scholarly expertise. IRB members are trained to adhere to the principles of Belmont Report in safeguarding the rights and welfare of human subjects and gain competence necessary for the review of specific activities proposed in a study. IRB members will be asked to fulfill many requirements of the IRB functions such as serving on IRB subcommittees, quality assurance and improvement activities and "for cause" and "not for cause" compliance activities of researchers and the IRB.

Institution's Deans or Department Chairs may nominate faculty and staff to serve on the IRB. The IO, and IRB Director may also approach Institutions Academic Deans and Department Chairs to nominate individuals for membership.

Students and medical residents may serve on the IRB; however, they must have the approval from their Academic unit heads.

Unaffiliated members are selected from the community. Such members may be clergies and retired employees who are not receiving formal compensation from the Institution.

The final decision in selecting a new member is made by the Institutional Official, in consultation with, IRB Chairs and IRB Director.

Each IRB member will be appointed for a term of three (3) years. Members may be reappointed for additional terms. In the event that a member steps down or is removed, the IO in consultation with IRB Director, and IRB chairs shall appoint a replacement member for the remainder of the unexpired term of a member replaced. Any member's unexcused absence for more than 50% of the regular meetings, or his/her lack of participation in the review of research projects to which a member is assigned during any academic year shall render the member subject to removal.

On an annual basis, the IRB Chair and the IRB Director and IO review the membership and composition of the IRB to determine if they continue to meet regulatory and institutional requirements. The IRB Chair in consultation with the IRB Director and IO may remove a member at any time.

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

- A. IRB meeting attendance;
- B. Number and/or quality of IRB reviews (both expedited and full board);

- C. Conduct during IRB meetings and
- D. Attendance at on-going educational activities

### **3.5 IRB Membership**

- A. Each of the IRBs is composed of at least five members and many alternate members. Members are selected based on the research objectives and corresponding expertise of the individuals.
- B. IRB members shall be sufficiently qualified, possess the professional competence through experience and expertise in safeguarding the rights and welfare of human subjects.
- C. Members complete Institution's web-based CITI IRB training modules specific to IRB members.
- D. A list of active IRB members will be maintained in the IRB office.
- E. IRB members shall be knowledgeable of the Institution's research policies and procedures, applicable laws, including FDA and DHHS regulations, and professional standards of conduct, practice, and procedure.
- F. IRBs consist of both men and women.
- G. They are not members of one profession.
- H. IRB shall include at least one (1) member whose primary interest is non-scientific, such as, a lawyer, university non-research personnel, educator or a member of the clergy.
- I. IRB shall include at least one (1) member who is not otherwise affiliated with the Institution and who is not part of the immediate family of any person affiliated with the Institution. The unaffiliated person could be a scientist or a non-scientist.
- J. The RowanSOM IRB (IRB #2) shall consist of at least one licensed physicians and other members with expertise in clinical, social, educational and behavioral sciences.
- K. The social and behavioral IRB shall consist of members with diverse expertise in social and behavioral sciences, business and information technology, but may not have licensed physician.
- L. If IRB reviews protocols involving prisoners, the IRB shall comprise of a prisoner advocate as a voting member. This member shall have the appropriate background to serve as the prisoner advocate. This member must be present at convened meetings when IRB conducts full board review.
- M. When considering protocols involving women, children, or other vulnerable persons as subjects, the committee shall have a voting member qualified to represent the group in question or shall avail itself of the advice of a qualified consultant or advocate.
- N. One member may satisfy more than one membership category.
- O. IRB may, at its discretion, invite "consultants" or "subject advocates" competent in special areas to assist in the review of issues that require special expertise, or to assist in gathering information on the issues raised by proposed research. Such

consultants or advocates are not IRB members. They have no authority to vote or take any official action on behalf of the IRB.

- P. The IRB Director and the IRB Coordinator(s) are voting member.

### **3.6 Alternate Members**

Alternate members are generally selected to substitute for a voting member. The appointment of an alternate member in general is based on what primary IRB member was intended to serve. Alternate IRB member has experience, expertise, background, professional competence, and knowledge comparable to that of the primary IRB member whom the alternate would replace. An alternate member may be present in a convened meeting; however, the alternate member shall vote only when a regular voting member is absent for the entire or part of the meeting. Alternate members are also appointed for a term of three (3) years and they may be reappointed for additional terms.

### **3.7 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. This is generally done through web-based CIRB review system. Members 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.

### **3.8 Member Conflicts of Interest**

An IRB member can be an investigator. In each IRB meeting, the Chair will determine whether any of the members have a conflict in reviewing protocols. No member of the IRB shall participate in any way in the initial or continuing review of any project in which the member has a conflict of interest as determined under governmental or institutional policies, except to provide information requested by the IRB. All IRB members sign a documentation that they will abide by the requirements of conflict of interest and confidentiality of matter discussed in the IRB meeting and IRB materials (**Appendix 10**). In the event that the Chair has the conflict, the Vice Chair or other senior member of the IRB shall preside the meeting.

The following circumstances may render members having conflict of interest for reviewing research:

- A. Where the member or consultant is involved in the design, conduct, and reporting of the research;
- B. Where an immediate family member of the member or consultant is involved in the design, conduct, and reporting of the research;
- C. Where the member holds significant financial interests related to the research being reviewed; and



- D. Any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a protocol.

All IRB members complete and sign the Conflict of Interest Form (**Appendix 10**)

### **3.9 IRB Subcommittees**

Some of the IRB functions may be performed by IRB sub-committees appointed by the Chair(s) of the IRB. 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. The number and composition of the IRB Subcommittee members shall depend on the authority delegated by the IRB Chair to such IRB Subcommittee. IRB subcommittees can create policies, investigate non-compliance and make appropriate recommendations to the full IRB. Only full IRB has the authority to approve, recommend conditions to be met for approval, table or recommend disapproval of protocols.

### **3.10 IRB Consultants**

When necessary, the IRB Chair or the IRB Director may solicit individuals from within the Institution 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. IRB consultants must be screened by the IRB Director or IRB Chair to not having the conflict of interest. If consultants have a conflict, they will be excluded.

The IRB Office will ensure that all relevant materials are provided to the outside reviewer prior to the convened meeting. Efforts will be made to protect the identity of the investigator and the confidential information.

Consultants provide their review to the IRB either in writing or in person, but will not participate in the vote. 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.

### **3.11 IRB Member Training**

The Institution is committed to train IRB members by requiring them to complete the specific CITI training for IRB members as well as continuing training through on going educational process in the IRB meetings (<https://www.citiprogram.org/members/index.cfm?pageID=50>). Members are required to complete CITI refresher training every three years.

New IRB members and alternates must complete CITI Training (IRB Members Module) and participate in the initial IRB member orientation process. The orientation process is a formal face to face training which includes the IRB Chair, the IRB director and the IRB

coordinator(s). The training includes the description of Belmont Principles, the Common Rule, FDA regulations, and Institution's human subject protection policies, conflict of interest policies and providing a copy of Institution's IRB Members Handbook.

Continuous ongoing training will be provided in the IRB meetings by updating the members with current and evolving regulations and guidance, ethical and scientific issues, institutional policies, procedures, opportunities to attend web-based workshops or conferences (PRIM&R) and providing them with copies of appropriate publications. If members are unable to attend some of the continuing educations, the IRB Director will provide a make-up session for those individuals. Those members who have not completed the continuing education, they will be asked to complete the education before otherwise they may not be allowed to review and vote.

### **3.12 Membership Records**

IRB records shall identify each member by name, earned degree (if any), representative capacity as individual affiliated or not affiliated, and specialty as physician scientist, other scientist, or nonscientist as required by regulations. In addition, IRB shall maintain records that identify each member by name; earned degree (if any); representative capacity; Institution or other affiliation and position; occupation; specialty; indication of experience, such as board certification and licenses (if any), sufficient to describe each member's anticipated contributions to the IRB deliberations; and any employment or other relationship between each member and the Institution. Any changes in the IRB membership shall be reported to the OHRP as required by regulations. All members shall provide their Curriculum Vitae at the time of appointment.

### **3.13 Insurance and Indemnity**

IRB members including unaffiliated members are protected with insurance coverage and are indemnified as provided by applicable Institutional policies.

### **3.14 Allegations and Undue Influence**

Institutions research team, faculty, staff, administration or students may report to the IRB office suspected or actual non-compliance with the provisions of the approved study as well as applicable human research regulations. Complaints can also be sent to the IO, HPA, IRB Director or any other senior administrators in the Institution(see Section 1.6 of this Guidance). Reports of noncompliance may arrive in the form of a complaint or from the results of audit.

Research participants, family members of research participants, and other external to the Institution, including regulatory agencies may also report in writing or anonymously suspected noncompliance to the IRB, Institution's Hot line, to the IO or to the President of the Institution.

The reports of research non-compliance, misconduct and whistleblower reports are subject to different rules and they may be referred to the Institution's Legal Counsel.

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

### **3.15 IRB Scheduled Meetings**

IRB shall conduct any necessary business that routinely involves the IRB responsibilities. IRBs will meet as frequently as is necessary to complete the business of the IRB, with meetings conducted by the IRB Chair, Vice-Chair, or appropriate designee of the IO, the IRB Director, Chair or Vice Chair.

### **3.16 Quorum**

Except when an Exempt or Expedited review process is followed (see Article 4.4 of these guidelines), the activities of the IRB and the review of research protocols may only be conducted at a meeting at which a quorum is present. A quorum shall be defined as a simple majority of the total membership of the applicable IRB that shall include at least one licensed physician (for medical IRB, IRB # 2) and at least one person whose primary interest is non-scientific. Efforts must be made to have one of the unaffiliated members present at most of the meetings. Alternate members are counted as voting members when a primary member is absent. On social and behavioral IRB, a non-scientific member will be identified at each of the meetings.

### **3.17 Telephone and Audio-visual (AV) use for meetings**

The Institution prefers face-to-face meetings. However, at times members may participate through telephone or audio-visual conference methods. When telephone and audio-visual methods are used, the minutes will reflect how members participated in the meeting. All members, irrespective of their mode of participation shall receive all pertinent information prior to the meeting and will be able to participate equally and actively during discussions. When a member leaves the AV conference, that member will not be counted towards the quorum. This policy is consistent with **FDA policy 46 CFR 8967, January 27, 1981**.

### **3.18 Reporting of regulatory changes and guidelines**

The IRB Director shall regularly report to the IRB any amendments to or newly applicable FDA or Common Rule regulations as well as any changes in the Institution's policies and procedures that affect the operation of the IRB and its ability to safeguard the rights and welfare of research subjects. The IRB Director shall also regularly report to the IO any amendments to existing regulations or newly applicable FDA and DHHS regulations, non-compliance/deviations in implementing protocols as approved by the IRB, suspensions and alleged scientific misconduct.

### **3.19 Meeting Procedures**

The IRB Chair, or Vice-Chair (in the event that the IRB Chair is absent or conflicted), 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, except in the case of a conflict of interest. Alternate members have full voting rights if the primary member is absent. In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting.

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

### **3.20 Guests**

Each Principal Investigator (highly recommended) or his/her representative 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 Institution's research may, 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 IRB Director. Guests, other than ex-officio guests, may not speak unless requested by the IRB. All guests, other than Principal Investigators or their designee, must sign a confidentiality agreement.

## ARTICLE 4 - IRB REVIEW PROCESS

Day-to-day operations of the activities are conducted in IRB offices at the institution's campuses. IRB offices uses an electronic Institutional Review Board (CIRB) for developing an IRB application form, administrative review of the electronic IRB submission, IRB reviews by the members and IRB approval process, continuing review final reports, adverse event reporting, and review of amendments to make changes.

All human subject research conducted under the auspices of the Institution must meet one of the following methods for review:

- A. Non-human subject research;
- B. Exempt Review;
- C. Expedited Review (Minimal Risk Study) and\*
- D. Full Committee Review

\*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.

### 4.1 Studies Eligible for Exempt Review

There is no deadline for submitting exempt review applications.

**Studies qualifying for Exempt category status are:**

1. **Category 1 - 45 CFR 46.104 (d) (1)** – Research conducted in established or commonly accepted educational settings, involving normal educational practices that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies and, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
2. **Category 2 - 45 CFR 46.104 (d) (2)** –Research only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedure, interview procedures or observation of public behavior (including visual or auditory recording) of at least one of the following criteria is met:
  - 45 CFR 46.104 (d) (2) (i)** - The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
  - 45 CFR 46.104 (d) (2) (ii)** - Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
  - 45 CFR 46.104 (d) (2) (iii)** -The information obtained is recorded by the investigator in such a manner that the identity of the human subjects' can readily be

ascertained. Directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination.

**Research falling under this Exempt category 2 (d) (2) (iii) will be reviewed by an IRB member who is qualified to conduct such review and the review will be conducted as an expedited review using one of the Expedited review categories.**

3. **Category 3 - 45 CFR 46.104 (d) (3) (i)** – Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording of the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:
  - (A) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
  - (B) Any disclosure of the human subjects’ responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation; or
  - (C) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects’ can readily be ascertained. Directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination. **Research falling under this category will be reviewed by an IRB member who is qualified to conduct such review. The review will be conducted as expedited review using one of the categories of Expedited review.**

**45 CFR 46.104 (d) (3) (ii)** - for the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having the, solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else,

**45 CFR 46.104 (d) (3) (iii)** if the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research. **The prospective agreement will be reviewed by an IRB member as an expedited review.**

4. **Category 4 - 45 CFR 46.104 (d) (4)** – Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, or at least one of the following criteria is met:

**45 CFR 46.104 (d) (4) (i)** -The identifiable private information or identifiable biospecimens are publicly available.

**45 CFR 46.104 (d) (4) (ii)** -Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subject, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

**45 CFR 46.104 (d) (4) (iii)** - The research involves only information collection and analysis involving the investigator’s use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of “health care operations” or “research” as those terms are defined at **45 CFR 164.501** or for “public health activities and purposes” as described under **45 CFR 164.512 (b)** ; or

**45 CFR 46.104 (d) (4) (iv)** - The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained from non-research activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208 (b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used or generated as part of the activity will be maintained in systems of records subject to the **Privacy Act of 1974, 5 U.S.C> 5552a**, and, if applicable, the information used in the research was collected subject to the **Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.** **Research falling under this category will be reviewed by an IRB member who is qualified to conduct such review. The review will be conducted as expedited review using one of the categories of Expedited review.**

5. **Category 5 - 45 CFR 46.104 (d) (5)** –Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits to services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies

under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as **sections 1115 and 1115A of the Social Security Act**, as amended.

**45 CFR 46.104 (d) (5) (i)** - Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such a manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

6. **Category 6 - 45 CFR 46.104 (d) (6)** - Taste and food quality evaluation and consumer acceptance studies:

**45 CFR 46.104 (d) (6) (i)** - If wholesome food without additives are consumed, or

**45 CFR 46.104 (d) (6) (2)** - If a food is consumed that contains a food ingredient at or below the level and 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.

7. **Category 7 - 45 CFR 46.104 (d) (7)** - Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determination required by 45 CFR 46.111 (a) (1-7). **Such research and the consent form will be reviewed by an IRB member as an expedited review. Investigators must use either the adult consent form version 06/18/2018 or Parental/Guardian Consent form version 2/10/2015 for collecting private identifiable information or identifiable biospecimens**  
**(<https://research.rowan.edu/officeofresearch/compliance/irb/submissions/consenttemplates/index.html>.)**

8. **Category 8 - 45 CFR 46.104 (d) (8)** - Secondary Research for which consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use if the following criteria are met:

**45 CFR 46.104 (d) (8) (i)** - Consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with **45 CFR 46.116(a)(1) through (4), (a) (6), and (d)**;



**45 CFR 46.104 (d) (8) (ii)** - Documentation of informed consent or waiver of documentation of consent was obtained in accordance with **45 CFR 46.117**.

**45 CFR 46.104 (d) (8) (iii)** - An IRB conducts a limited IRB review and makes the determination required by **45 CFR 46.111(a)(7)** and makes the determination that the research to be conducted is within the scope of the consent referenced in paragraph **45 CFR 46 (d) (8) (i)** of the section; and

**45 CFR 46.104 (d) (8) (iv)** The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results. Such research and the Broad consent will be reviewed by an IRB member as an expedited review.

**Research for which LIMITED IRB REVIEW is a condition of exemption under 45 CFR 46.104 (d) (2)(iii), (d)(3)(I)(C), and (d)(7) and (d) (8) listed above will be reviewed at expedited review level.**

**For Exempt review categories 7 and 8, the IRB has chosen not use a broad consent instead to use Adult consent or Parent/Guardian consent forms.**

Research activities that are permitted under exempt categories for Subparts, B, C and D are:

**Subpart B:** Research with pregnant women and neonates are allowed if the conditions of the exception are met.

**Subpart C:** Research using prisoners is not allowed except for research aimed at involving a broader subject population that only incidentally including children is approved for exempt category 1, 4, 5, 6, and 7 (listed below) if the conditions for exemption are met.

**Subpart D:** Research with children is allowed for exempt category 2 for educational tests or the observations of public behavior when the investigators do not participate in the activities being observed. Research with children is not allowed as exempt when the information obtained is recorded in a manner that the identity of the person can be readily obtained.

#### **4.2 FDA Exemptions**

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

FDA regulations at §56.104 exempt the following categories of clinical investigations from the requirements for IRB review and approval, although the activities require an exempt determination or IRB notification.

- A. Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided

that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before July 27, 1981.

- B. Any investigation commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under Food and Drug Administration regulations before that date.
- C. 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.
- D. 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  
**[46 FR 8975, Jan. 27, 1981, as amended at 56 FR 28028, June 18, 1991].**

#### **4.3 Procedures for Determining Exemption**

In order to determine whether the proposed project is eligible for exemption, investigators must complete the online CIRB initial application with appropriate attachments as required in the CIRB submission module. Investigators receive electronic notices when the CIRB application is incomplete. If research materials are coming from another site, appropriate letter from the source must be attached or uploaded to the application. The IRB office will verify current human research protection training for all members of the research team.

The designated IRB member, IRB Chair or the IRB Director or his designee who is also an IRB member reviews all 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 must not have any apparent conflict of interest. The reviewer will determine the exempt status by completing an exemption determination form and the checklist on CIRB. The reviewer will also determine whether the exempt application meets the definition of human subject research. When approval is granted, the reviewer will determine the category under which the exemption was approved. Exempt studies are communicated to the IRB, at a convened meeting. Continuing Review is NOT required for Exempt Studies unless under the new common rule certain studies requiring limited review or review of consent that involves the use and storage of identifiable private information or identifiable bio-specimens a continuing review or progress would be required since such studies are reviewed as expedited review.

#### **4.4 Studies Eligible for Expedited Review**

The IRB may use the expedited review procedure to review minor changes or amendments for previously full board-approved research during the period for which approval is authorized for one year or less.

Expedited review will be used whenever regulations require limited review or use of broad consent to use and store identifiable private information or identifiable bio-specimen for secondary research purposes.

Expedited review may be used for protocols in which enrollment has been completed or protocols in which enrollment have not occurred Expedited review is not used for studies approved by the full board.

Expedited review will not be used for classified research. Other than the exception stated above, only studies involving "minimal risk" to subjects may receive Expedited review. There is no deadline for submitting expedited review applications.

"Minimal risk" means that the risks of harm anticipated in the proposed research are not greater, considering probability and magnitude, than those ordinarily encountered in daily life or during the performance of routine physical and physiological examinations or tests (noninvasive examples, physical, blood pressure, EKG). Research projects involving unhealthy subjects (adults and minors) are not eligible for expedited research.

#### **4.5. Categories of Research Eligible for Expedited Review**

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. For additional guidance go to the following link:

<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-expedited-review-procedures/index.html>.

Research Categories one (1) through seven (7) below 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, non-pregnant 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 Common Rule 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.]

Please note that expedited review usually is not appropriate at the time of continuing review if the research required review by the convened IRB at the time of initial review.

#### **4.6 Procedures for Expedited Review**

In order to determine whether the proposed project is eligible for expedited review investigators must complete the online CIRB initial application with appropriate attachments as required in the CIRB submission module. Investigators receive notices when the CIRB application is incomplete. If research materials are coming from another site, appropriate letter from the source must be attached to the application. IRB office will verify current human research protection training for all members of the research team.

Expedited 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 designees must be a voting member of the IRB. 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), will receive and review all documentation that would normally be submitted for a full-board review. These documents may include, the protocol, the consent form, the financial disclosure form, survey instruments, data collection instruments, recruitment materials and process and any other materials that may be important information for the expedited review.

For continuing reviews or progress reports, the investigator will submit a continuing review form or progress report. An annual financial conflict of interest form is required for continuing review.

In reviewing the research, the reviewers 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.

At the time of the initial review reviewers may make a determination whether a continuing review is required by providing appropriate rationales for requesting a continuing review, require modifications or require a convened board to conduct the protocol review/initial review form. If modifications are required, the IRB Office staff will inform the investigator through electronic communication via CIRB.

Unless an IRB determines otherwise, continuing review of research is **not required** in the following circumstances **(45 CFR 109(f)(1))**:

- a. Research eligible for expedited review in accordance with **45 CFR 46.110 (45 CFR 46 109 (f) (1)(i))**;
- b. Research reviewed by the IRB in accordance with the limited IRB review described in **45 CFR 46.104(d)(2)(iii), (d)(3)(i)(c), or (d)(7) or (8)**;
- c. Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
  - (i) Data analysis, including analysis of identifiable private information or identifiable biospecimen, or
  - (ii) Accessing follow-up clinical data from procedures that subjects would undergo as part of the clinical care.

If the reviewer decides that an annual progress report is required, a progress report must be submitted or close the study using final report on the CIRB.

Investigators will also be informed that if a progress report is required. If the study is continuing, any modifications to the study must be reported and such modifications can only implemented after the IRB approval.

If progress report is required and if unanticipated adverse events occur, such events must also be reported.

If study is not continuing and not closed, such non-compliance will be reported to the IO and the Dean of the respective faculty including preventing review of new submission of that particular investigator until the expired study has been closed.

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

Members of the IRB will be apprised of all expedited review approvals by means of a list in an agenda within a month of the expedited approval. Any IRB member can request to review the full protocol by contacting the IRB office.

#### **4.7 Full Board Reviews (Convened meetings)**

##### **4.7.1 Meeting Schedules**

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 IRB website. Special meetings may be called at any time by the IRB Chair or the IRB Director.

##### **4.7.2 Administrative Review**

In order to determine whether the proposed project is eligible for full board review, investigators must complete the online CIRB initial application with appropriate attachments such as protocol, consent form, recruitment material, advertisements, etc. as specified and required in the CIRB submission module. If research materials are coming from another site, appropriate letter from the source must be attached to the application. IRB office will verify current human research protection training for all members of the research team including HIPAA training.

The IRB staff will 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 electronically on the CIRB as a “determinations letter” requirements to place the study in that month’s IRB agenda. If the determination letter is not responded to, the material study will not be placed on the agenda until a proper response is received by the IRB office.

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 either verbally or through an email, detailed information is needed to provide appropriate IRB guidance. Individual appointments with the IRB staff can also be arranged and are strongly recommended for first-time submissions.

##### **4.7.3. Assigning Primary and Secondary Reviewers**

After the administrative review for completeness, the IRB staff with the assistance of the IRB Director or IRB Chair assign protocols to primary and secondary reviewers. Reviewers are selected based on the scientific content of the protocol and corresponding expertise of the reviewer’s area of expertise with careful attention to vulnerable population to be included in research. A primary and a secondary reviewer will be



assigned to each protocol. A reviewer may be assigned to review more than one protocol, continuing review or modifications and reportable events. An outside consultant may be sought if the IRB does not have adequate expertise to review a protocol. Even when adequate expertise is available, but the member with scientific expertise or expertise to review risks to vulnerable population such as prisoner to review a protocol is not attending the meeting, such protocols may be deferred to another meeting.

The primary and secondary reviewers are responsible for:

- a. Having a thorough knowledge of all of the details of the proposed research.
- b. Performing an in-depth review of the proposed research.
- c. 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 (Article 3.7 of this guidance).
- d. Making suggestions for changes to the proposed research, where applicable.
- e. Completing all applicable IRB reviewer forms.
- f. The reviewers may discuss the protocol materials with the PI(s) to clarify any issues that may be raised; however the names of the reviewers are not voluntarily disclosed.

If both the primary and secondary reviewers are absent and an alternate member assigned to the primary member is available, he/she may review the protocol. Absent members can submit their written comments for presentation at the convened meeting. It should be noted that all of the IRB members review and are expected to review all studies, not just the ones they are responsible for reviewing. All items on the agenda are viewable by all members on the CIRB site, irrespective of the reviewer status.

#### **4.7.4 Pre-Meeting Distribution of Documents**

All required materials need to be submitted (in full) through CIRB 10 business days prior to the convened meeting for inclusion on the IRB agenda. The meeting agenda will be prepared by the IRB office staff under the supervision of the IRB Director or IRB Chair or both and the agenda will be electronically distributed. All IRB members will be notified electronically to review all IRB submissions. All IRB members can review materials which include the IRB agenda; prior month's meeting minutes, applicable business items, audit reports, if any, unanticipated adverse events, if any, appropriate continuing education materials, if any and protocol review materials no later than five (5) business days before the scheduled meeting. The intent is to allow sufficient time for the review process. Exceptions may be made by the IRB chair/IRB director requiring a prompt review due to extraneous circumstances.

#### **4.7.5 Materials received by the IRB**

Each IRB member will have complete access on CIRB website to all of the documents submitted to the IRB. These documents include the following items:

- A. Complete Application form;
- B. Protocol;
- C. Proposed Consent / Parental Permission / Assent Form(s);

- D. Recruitment materials / subject information; and
- E. Data collection instruments (including all surveys and questionnaires).

IRB members are notified whenever new documents are submitted.

Primary and Secondary reviewers are directed to review relevant grant applications; research protocol or 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), recruitment material and recruitment process, survey questionnaire or data collection instruments

All IRB members have access to all protocols at any time. If an IRB member requires additional information to complete the review, they may contact the IRB Office or directly contact the principal investigator to make the request of for such additional information. Reviewers must use a reviewer checklist(s) as a guide to completing their review. There are number of checklists to be completed by the reviewer based upon the study.

#### **4.7.6 Criteria for IRB Approval of Research**

In order for the IRB to approve human subject's research, either through expedited review or by the full IRB, it must determine that the following requirements are satisfied:

- A. 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.
- B. 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.
- C. 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.
- D. Informed consent will be sought from each prospective subject or the subject's legally authorized representative or a surrogate, in accordance with, and to the extent required by the Federal Regulations and University policy.
- E. Informed consent will be appropriately documented, in accordance with, and to the extent required by the Federal Regulations.

- F. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- G. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- H. 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.

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

#### **4.7.7 Risk/Benefit Assessment**

Risks may appear in multiple forms. Pain, discomfort or injury or possible side effects of drugs are part of physical harms. Participation in research may also subject to psychological harms such as changes in thought process and emotion (episodes of depression, confusion or hallucination resulting from drugs, feeling of stress, guilt and loss of self-esteem). While some psychological risks are minimal or transitory, it is the IRBs responsibility to be aware that some psychological risk has the potential for causing serious psychological harm.

Invasion of privacy is a risk of a somewhat different character. In the research context, it usually involves either covert observation or "participant" observation of behavior that the subjects consider private. The IRB will make two determinations (1) is the invasion of privacy acceptable in light of the subjects' reasonable expectations of privacy in the situation under study; and (2) is the research question of sufficient importance to justify the intrusion? The IRB will also consider whether the research design could be modified so that the study can be conducted without invading the privacy of the subjects.

Breach of confidentiality is sometimes confused with invasion of privacy, but it is really a different problem. Invasion of privacy concerns access to a person's body or behavior without consent; confidentiality of data concerns safeguarding information that has been given voluntarily by one person to another. The IRB will determine that a breach of confidentiality may result in psychological harm to individuals (in the form of embarrassment, guilt, stress, and so forth) or in social harm.

Social and economic harms may arise from invasions of privacy and breaches of confidentiality. It generally results in embarrassment within one's business or social group, loss of employment, or criminal prosecution. In such case, the IRB will determine how to safeguard against such harm.

The goal of risk 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. To accomplish that the IRB must:

- A. 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;
- B. 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:

- a. Identify the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research;
- b. Determine whether the risks will be minimized to the extent possible;
- c. Identify the probable benefits to be derived from the research;
- d. 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;
- e. 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:

- a. By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk; and
- b. 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.

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. In the case of studies that fall under expedited review, the reviewer shall determine whether a continuing review is required for the material study being reviewed. If the reviewer decides that a continuing review is required, the reviewer shall provide sufficient reasons why a continuing review is required. The IRB chair may review the continuing review requirements whether to proceed with a continuing review or not. The decision to change the continuing review may occur at the initial review or subsequent continuing review based on the periodic progress report.

#### **4.7.8 Scientific Merit**

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

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

#### **4.7.9 Equitable Selection of Subjects [45 CFR 46.111(a)]**

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.

#### **4.7.10 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. Guidance to recruiting subjects in a clinical trial is provided in the following links:

<https://www.fda.gov/RegulatoryInformation/Guidances/ucm126428.htm>. and <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/clinical-trial-websites/index.html>.

The investigator shall consider the following variety of factors to recruit research subjects:

- A. Requirements of scientific design;

- B. Susceptibility to risk;
- C. Likelihood of benefits and what they might be;
- D. Practicability of recruiting subjects; and
- E. Fairness – Since a primary aim of clinical research or social and Behavioral research is to provide scientific evidence leading to a change in health policy or a standard of care, or social or behavioral studies.

In addition, it is imperative to determine whether:

- A. The intervention or therapy being studied affects women, children, or men and populations of minority groups differently;
- B. Equitable selection of subjects and the applicability of study results generally require investigators to strive for gender balance in the study population.
- C. Women, children, and members of minority groups must be included in all research projects involving human subjects unless a clear and compelling justification establishes to the satisfaction of the IRB that inclusion is inappropriate with respect to subjects or the purpose of the research;
- D. If a proposed project includes a study population in which women and minorities are not appropriately represented, the PI must provide “a clear compelling rationale for their exclusion or inadequate representation.”
- E. Factors such as inconvenience (e.g., time required, travel involved, or restrictions on diet or other activities), discomfort, and embarrassment and burdens of participating in research that may also be considered in planning study enrollment;
- F. Detailed procedures for subject recruitment and selection as follows:
  - i. Provide the number to be recruited at this institution and elsewhere (multicenter studies), ages, and sex of prospective subjects and
  - ii. Describe any inducements or remuneration to be offered to subjects (e.g., cash payments, free hospitalization, medication, clinical testing).
- G. Detailed methods of recruitment to ensure subjects from a variety of sources have chances of being selected, such as:
  - i. Notices on bulletin boards and advertisements to encourage participation of subjects from a broad cross Article of the community or personally recruit subjects from community health clinics.
  - ii. Provide the name of the hospital and the inpatient service, or the recruitment site and letter of authorization for the recruitment site.
  - iii. Outpatient clinic, school, business, or other agency from which subjects will be recruited.
  - iv. Indicate any “special” or “vulnerable” categories of subjects, i.e., mentally disabled persons, minors, pregnant women, and prisoners.
- H. IRB does not approve finder’s fees in research studies. Finder’s fees are any payments to physicians or other professionals for referring individuals to research studies.
- I. Contacting prospective participants is not acceptable unless specifically approved by the IRB.

- J. A physician who has a treatment relationship with a prospective research subject may approach that patient about participation in an IRB approved protocol.
- K. If a researcher wants to contact a potential patient managed by another physician, the potential subject's physician must give approval before the patient is contacted.
- L. If a researcher wants access to a potential subject's contact information and/or records to invite the subject to participate, the researcher must secure permission from the Privacy Officer through the use of Preparatory to Research Form ([https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1\\_27](https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1_27). ) and must receive approval from the subject's physician or physician's department head (if the physician is no longer in the institution) and the IRB to contact the prospective subject or prospective subject's records.

#### **4.7.11 Informed Consent**

The IRB will ensure that informed consent will be sought from each prospective subject; his/her surrogate (in accordance with surrogate consent guidance waiver); 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 and **21 CFR 50.27**. See Article 5 of this guidance for detailed policies on informed consent.

#### **4.7.12 Safety Monitoring**

For all research that is more than minimal risk, the investigator must submit a safety monitoring plan when required by the IRB. This is required for clinical trials, but does not exclude social and behavioral studies where the risk is anticipated to be high. 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:

- A. Monitoring is commensurate with the nature, complexity, size and risk involved.
- B. Monitoring is timely. Frequency should commensurate with risk. Conclusions are reported to the IRB.
- C. 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.

For an individual Safety Monitor the plan must include:

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

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

- a. The name of the Data Safety Monitoring Board;
- b. Where appropriate, is independent from the sponsor;
- c. Availability of written reports;
- d. 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 clinician's knowledgeable about the disease and treatment under study should be part of the monitoring group or be available if warranted;
- e. Frequency and content of meeting reports and
- f. 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/Committee (DSMB/C) 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 DSMC. 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 DSMCs 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.



For further guidance on data safety monitoring go to the following links:

<https://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127073.pdf>

. and <https://grants.nih.gov/grants/guide/notice-files/NOT-HS-11-015.html>.

#### 4.7.13 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.

##### 4.7.13.1 Definitions

**Confidentiality** - methods used to ensure that information obtained by researchers about their subjects is not improperly divulged.

**Identifiable information** – is identifiable private information for which the identity of the subject is or may be readily ascertained by the investigator or associated with the information.

**Identifiable Biospecimens** – is a biospecimen for which the identity of the subject is or may be readily ascertained by the investigator or associated with the biospecimen.

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

Private information.

**Private information** includes information about behavior that occurs in a context in which individual can reasonably expect that no observation or recording is taking place and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public.

##### 4.7.13.2 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 subject's 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:

- A. Methods used to identify and contact potential participants or their private identifiable information or identifiable biospecimens;
- B. Settings in which an individual will be interacting with an investigator;
- C. Appropriateness of all personnel present for research activities;
- D. Methods used to obtain information about participants or their biospecimens and the nature of the requested information or biospecimens;
- E. Information or biospecimens that is obtained about individuals or their biospecimens 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) and

- F. How to access the minimum amount of information necessary to complete the study.

#### **4.7.13.3 Confidentiality**

Confidentiality and anonymity are not the same. If anyone, including the investigator, can readily ascertain the identity of the subjects from the data or biospecimens, 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 must ensure that the privacy and confidentiality of research subjects is protected. The IRB shall assess whether there are adequate provisions to protect subject privacy and maintain confidentiality. The IRB shall do 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 or biospecimens;
- D. The methods to protect the confidentiality of research data and biospecimens.

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 shall 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 and biospecimens.

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 or biospecimen 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.

#### **4.7.14 Vulnerable Populations**

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

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

#### **4.7.15 Studies Involving Multiple Diseases**

If a study involves multiple targeted diseases, separate protocols and separate consent forms must be submitted for each of the targeted diseases. An omnibus protocol for multiple studies is not permitted.

### **4.8 Additional IRB Considerations During Review and Approval**

#### **4.8.1 Duration of Approval**

At the time of initial approval and continuing review (if required by the IRB), the IRB shall determine the specific annual date or expiration date for review and provide written notice to the PI. Continuing review for projects that fall under expedited review categories may not be necessary unless the reviewer at the time of the initial review provides reasonable explanation why a continuing review is required. 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 few 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 date is the date in which the study was approved with conditions or stipulation. For a study that was deferred or tabled, the approval date will be the date in which the IRB approved the study or approved with conditions or stipulations.

For a study approved under expedited review, the approval period begins on the date the IRB Chair or IRB member(s) gives final approval to the protocol.

The approval date and approval expiration date are clearly noted on all IRB approval letter sent to the PI. The expiration date must be strictly adhered to. The CIRB automatically sends reminders to submit the continuing review or progress reports 90, 60 and 30 days before the expiration date. This allows investigators sufficient time to develop and submit renewals.

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 IRB will also determine whether a particular research proposal, because of the degree of risk or for any other applicable reason to the subjects, mandates IRB re-review

more often than the minimum annual review. Such risks may include the degree of uncertainty regarding the risks involved, the vulnerability of the subject population, the experience of the investigator, the IRB previous experience with the investigator and or sponsor, the projected rate of enrollment whether the study involves the use of novel therapy or device. If more frequent review is deemed appropriate, the IRB will notify the PI in writing with the initial approval. More frequent review may be requested by the IRB as required during the progress of an investigation, particularly for review of unanticipated adverse events. The meeting minutes will reflect the IRB's determination regarding review frequency.

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 5 pm of the date when IRB approval expires. Detailed information is provided in Articles 4.0 to 4.10.6 of these guidelines when protocol has expired/lapsed. The IRB will send 90, 60 and 30 day notices to investigators to initiate the continuing review or study closeout.

#### **4.8.2. Reasons for Increased Frequency of Review**

More than an annual review of a study may be required when research meeting any of the following criteria:

- A. 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;
- B. The involvement of especially vulnerable populations likely to be subject to coercion (e.g., terminally ill);
- C. A history of serious or continuing non-compliance on the part of the PI and
- D. Probability and magnitude of risk likely to be at high level, medical conditions of proposed subjects, qualification and experience of study team, nature and frequency of adverse events, novelty of a project with a high likelihood of unanticipated adverse events and any other factor that the IRB deems relevant.

If the decision of the IRB is to conduct reviews more often than an annual review, the IRB will determine either the frequency of review or number of subjects enrolled or studied. In both cases, the overall period of approval will not exceed one year. The reasons for increased frequency of review will be documented in the minutes and communicated to the investigator.

#### **4.8.3 Verification of Compliance with Approved Protocols from Sources Other than the Investigator**

IRB has the responsibility to conduct ongoing monitoring of approved research, the IRB may, as appropriate, independently inquire into allegation of non-compliance and verify that research is being conducted in accordance with approved protocols and/or that study procedures are not harming subjects.

The IRB may undertake independent verification in circumstances including but not limited to the following:

- A. To assure that no material changes have occurred since the previous IRB review
- B. If the study involves experimental therapies or procedures in which a clear potential for significant adverse experiences has been identified at the time of review
- C. If complaints from a subject or a third-party are received
- D. If one or more of the investigators has/have an actual or apparent conflict of interest
- E. If there is allegation of scientific misconduct
- F. If the nature and frequency of adverse events observed in similar research, or the nature and frequency of adverse events observed in the protocol under review, warrants concern and/or if the study involves a vulnerable population, including those who may be unfamiliar with the language on consent forms and other documents
- G. If there is allegation that research activity is being or has been conducted without IRB approval.

In circumstances listed above, the IRB chair, or the IRB director, will review the information from the investigator as well as other sources and determine if further investigation is necessary.

#### **4.8.4. Monitoring Consent Process**

To ensure that the consent process is appropriate and the approved process is being followed, the IRB may on occasion determine that special monitoring of the process must occur. Such monitoring is deemed necessary for the IRB to meet its responsibilities to ensure human subject protections for research that presents significant risk.

The IRB has the authority to observe or have a third party observe the consent process and the research [45 CFR 46.109(g)].

In reviewing the adequacy of proposed informed consent procedures, the IRB will determine on a protocol-by-protocol basis as a part of the initial and continuing review process those protocols that require third party observation/monitoring of the consent procedures. The person(s) authorized to conduct the monitoring will be identified by the IRB Chair in collaboration with the IRB director, and the meeting minutes will document these plans. The monitoring results will be reported to the IRB that requested the monitoring and reflected in the minutes, and the monitoring report will be included in the protocol file. If the initial determination requiring third party observation/monitoring of the consent procedures was open-ended, when the IRB determines that the monitoring is no longer required, the minutes will record that determination.

#### **4.8.5 Investigator Conflicts of Interest**

In order to ensure adequate protection of research subjects, it is imperative that investigators with conflicts of interest declare those conflicts for review by the IRB. The CIRB application has a specific form for investigators to complete and declare their conflict of interest (**Appendix 10**). In addition to the IRB, the conflict of interest committee will determine if there is a disclosure of the potential Conflict of Interest that may have an impact on subjects. The decision will include what course of action, if any, will be required of the investigator to mitigate such conflicts. If a financial conflict of interest exists, final IRB approval of a protocol cannot be given only when approved conflict management plan as decided by the conflict of interest committee. Continuing review of full board approved IRB studies, an annual conflict of interest form (<https://sites.rowan.edu/officeofresearch/compliance/conflictinterest/conflictforms/index.html>) must be submitted. Studies that require **annual progress report do not** require submission of a conflict interest form unless there is change in the personnel or there is a change in terms of conflict for previously approved investigators. An amendment to the study must be made noting these changes along with a completed conflict interest form for review and approval. Whenever such modifications are submitted, changes to the study cannot be implemented until the IRB approves such modification to the study.

#### **4.8.6 Significant New Findings**

During the course of a study, the IRB may review reports generated from adverse events, current literature, and other sources to ascertain the status of the study and assess whether or not the risk/benefit balance is still acceptable, whether or not new information needs to be conveyed to subjects, or if a segment of the population may be bearing an undue burden of research risk or being denied access to promising therapy. PIs are required to report any significant new findings to the IRB. 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, reviewed and approved by the IRB and the IRB may require that the currently enrolled subjects may have to be re-consented. Subjects must acknowledge the receipt of this new information and affirm their continued participation.

#### **4.8.7 Advertisements**

Advertising for subjects may include but is not limited to radio, television, Internet, billboards, bus signs, Facebook, Craigslist, etc. The IRB must approve the content of all recruiting advertisements for all research studies. An exact copy of the statements and graphics noted in advertisements must be provided to the IRB. Advertisements should not contain any promises about outcome or promise of direct benefit or other potentially misleading information. Advertisement on Facebook or any other social media cannot be direct. The principle investigator shall provide a secondary means such as a website to provide additional information, consent, etc. so the proprietary information is not posted

in the social media. This is done to protect the intellectual property of the proposed project.

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:

- A. Statements implying a certainty of favorable outcome or other benefits beyond what was outlined in the consent document and the protocol;
- B. Claims, either explicitly or implicitly, that the drug, biologic or device was safe or effective for the purposes under investigation;
- C. Claims, either explicitly or implicitly, that the test article was known to be equivalent or superior to any other drug, biologic or device;
- D. Using terms like “new treatment,” “new medication,” or “new drug” without explaining that the test article was investigational;
- E. Promising “free medical treatment” or behavioral or other forms of treatments when the intent was only to say participants will not be charged for taking part in the investigation;
- F. Emphasis on payment or the amount to be paid, such as bold type or larger font on printed media and
- G. 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:

- A. The name and address of the investigator and/or research facility;
- B. The condition being studied and/or the purpose of the research;
- C. In summary form, the criteria that will be used to determine eligibility for the study;
- D. The time or other commitment required of the subjects;
- E. The location of the research and the person or office to contact for further information;
- F. A clear statement that this is research and not treatment;
- G. A brief list of potential benefits (e.g. no cost of health exam) and
- H. 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.

For additional information on advertising at RowanSOM, please go to:

[https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/advertisingrecruit.html#p7EPMc1\\_16](https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/advertisingrecruit.html#p7EPMc1_16).

#### **4.9 Payment to Research Subjects**

PIs must balance conflicting considerations in making decisions about recruitment of subjects and payments intended to encourage participation or compensate subjects for their time, expenses and inconvenience. It may be necessary to offer a stipend in order to recruit volunteer subjects; however, payment should not be considered as a benefit. Payments to research subjects may also take various forms including but not limited to personal items, cash, gift certificates and raffles. However, the amount offered should not be so great that it exerts undue influence or becomes coercive. A payment should not financially induce a subject to participate in research that may be adverse to his/her interests or contrary to his/her wishes. The PI should also consider that overly generous stipends might encourage individuals to lie or conceal information that would disqualify them from the study.

When payments are made in the form of cash, subjects should be made aware that when cash is offered, the institution may have to report such cash offers to appropriate authorities which may result in disclosure of their personal information to such authorities. The IRB will review the amount and proposed method of payment to prevent coercion or undue influence.

If payment is offered, it must be payable on a pro-rated basis to subjects who fail to complete the study for reasons beyond their control. The consent should state the basis on which compensation is calculated if the subject chooses to withdraw. If a payment may be totally forfeited, the reasons must be stated prominently in the consent form. Payments also should be structured so that they do not encourage a subject to fail to report side effects.

Payments when recruiting children as research subjects presents special concerns. Ordinarily, payments offered to parents should be limited to reimbursement for expenses, such as carfare, parking, or baby sitters for siblings, so as not to give the parent an ulterior motive to volunteer the child for the study. If the research involves painful procedures, lengthy interviews, or self-administered tests, it may be appropriate to offer younger children a small payment in the form of one or more toys of appropriate value or a gift certificate for a restaurant.

There is no prohibition against offering appropriate payments to students or employees participating in research, but PIs must take care that recruitment is not deceptive, coercive, and that the research does not interfere with students' classes or employee work duties. Recruitment and payment to students will be carefully reviewed by the IRB.

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).

#### **4.10 Committee Action**



After completing review of a research protocol based upon the procedures and criteria described in this guidance, the convened IRB may take any of the following actions as described below.

#### 4.10.1 Convened Meetings

- A. **Approved:** At a convened meeting, the IRB may approve a study as submitted. The PI will be sent a notice of approval through CIRB.
- B. **Changes Required:** At a convened meeting, the IRB reviewed and approved the research protocol provided that the PI makes change(s) required by the IRB and/or makes minor change(s) to secure approval.
- C. **The PI will be informed through CIRB required conditional changes indicating that the research protocol has been reviewed and may receive approval contingent upon the PI making the required changes to secure approval. The revised study when uploaded into CIRB, will be reviewed by the Chair or his/her designee. If the revisions are satisfactory, an approval notice will be sent to the PI through CIRB. The approval date is the date in which the IRB approved the study with conditions. The study must not be initiated until IRB approves the study.**
  - a. **Tabled or No Action Taken:** At a convened meeting, the IRB reviews the research study and may table the study to be reviewed at another meeting due to insufficient information for the IRB to conduct a review. The reasons for insufficient information may include the following:
    - i. Minimization of risks to subjects;
    - ii. Reasonableness of risks in relation to benefits as well as knowledge resulting from the research;
    - iii. Equity of subject selection;
    - iv. Consenting process;
    - v. Data monitoring;
    - vi. Subject privacy and confidentiality of data;
    - vii. Additional safeguards needed for subjects likely to be vulnerable to coercion or undue influence (e.g. children, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons) and
    - viii. Ethical concerns.

The PI will be sent a notice indicating that consideration of the research protocol for approval has been tabled until the PI revises the protocol in such a way as to satisfactorily address the IRB's request for additional information about the factor(s) of concern.
- D. **Deferred:** At a convened meeting, the IRB reviews the research study and may table the study to be reviewed at another meeting due to insufficient information for the IRB to conduct a review. The PI will be sent a notice why the protocol has been deferred/tabled through CIRB process. Tabled and Deferred has similar meanings.
- E. **Disapproved:** At a convened meeting, IRB reviews and disapproves the Study. The PI will be sent a disapproved notice through CIRB process.

#### **4.10.2 Non-Convened Meetings**

Under an expedited review procedure, the review will be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among the members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. The IRB Chair or designee may approve the study as submitted or the reviewer may request changes to the study. When changes are made, the IRB Chair or designee may re-review and approve the study. Under the expedited review procedure the reviewer may require a continuing review. In such cases, the reviewer will provide a detailed rationale for requiring a continuing review.

When studies are sent to WIRB, the IRB director shall conduct an administrative review. Investigators are required to follow WIRB committee actions, policies and procedures.

#### **4.10.3 Proposed Changes in Research (Modifications)**

Investigators are allowed to make modifications to the approved protocols, but they must obtain approval before implementing the changes irrespective of the level of review. If changes are made are necessary to mitigate immediate danger to participants, IRB must be immediately notified. In order to secure approval for modifications/amendments to a protocol, investigators must submit an electronic version of the modification form with revised protocol, consent/parental permission form, recruitment material and other relevant documents as attachments. Modifications must be submitted as they are received from the sponsor or when the PI deems such a change is necessary. Modifications should be submitted prior to a continuing review as they are required to be reported as they occur and all approved modifications to the protocol need to be re-reviewed at the time of the continuing review.

After administrative review, the IRB Chair/IRB Director determines whether proposed changes may be approved by an expedited procedure or in a convened meeting. If the proposed changes are reviewed by the full board, all members will be notified and will have access to the proposed changes on the CIRB database. Two reviewers will be assigned to review modifications. The reviewer will lead the discussion. The reviewer will complete the checklist to determine whether the proposed changes are acceptable. Modifications, after review may be approved as submitted, may be deferred and moved to next meeting, tabled due to insufficient information, request for changes then re-reviewed either in a convened meeting or re-review by IRB chair or designees, approved by the IRB or denied approval. In all cases, IRB will determine whether proposed changes meet the regulatory requirements. IRB will also determine how the modifications will affect participants who are already enrolled, what information should be provided to them and by whom and provide an option whether participants want to continue participating in the study.

#### **4.10.4 Minor Changes**

An IRB may use expedited review procedures to review minor changes in ongoing previously-approved research during the period for which approval is authorized. A minor change is defined to have no substantive effect upon an approved protocol or reduce the risk to the subject.

Examples of minor changes are:

- A. Changes in research personnel that do not alter the competence of the research team to conduct the research (can be approved by the IRB coordinator);
- B. Scientific and/or therapeutic changes that leave the research population at the same or lower risk than risk(s) already approved;
- C. A minor increase or decrease in the number of participants (<25% change) or a >25% increase in the number of participants to be enrolled, but the number of participants to be “treated” remains the same. (e.g. – increase in number consented due to higher than expected rate of screen failures) or a larger % increase in number of subjects which does not affect the statistical plan;
- D. Changes in research procedures that have a minor impact on risks of harm, such as changes in the amount and frequency of blood draws (which remain within expedited criteria), addition of a clinic visit that involves no new procedures, or addition of a questionnaire that does not introduce new subject matter;
- E. An increase in the number of study visits for the purpose of increased safety monitoring;
- F. Minimal changes in remuneration;
- G. Changes to improve the clarity of statements, enhance comprehension or to correct typographical errors, updating to current template, without altering the content or intent of the statement and
- H. Clarification of discrepancies within the IRB review materials (protocol cover sheet, protocol, consent) such as the number of subjects, number and identity of research sites, timing, nature, and duration of research procedures.

In reviewing the research, the reviewers may exercise all of the authorities of the IRB. In circumstances where modifications are substantive elevating the risk to more than minimal risk, the study will be sent to full board review. The IRB Chair or designee may approve the modification as submitted. The reviewer may request changes to the modification. When changes are made, the IRB Chair or designee may re-review the modification and if the modifications are acceptable the reviewers they may approve the modification. The reviewer may require full IRB review since modifications may increase the level of risk. In all cases, the reviewer(s) complete the modification reviewer checklist on CIRB 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.

#### **4.10.5 Major Changes**

Major changes are changes that increase the research population's risk or are of questionable risk. Examples of major changes that are considered to increase the risk to the subject:

- A. Knowledge of a new risk which might affect the risk/ benefit ratio (for example, if a risk that is serious, life-threatening, or could potentially result in permanent disability). The addition of these sorts of risks might affect the IRB's view of the risk/benefit ratio and should therefore be reviewed by the full board;
- B. Increasing the length of time the subject is exposed to experimental aspects of the study;
- C. Increasing the dose/strength of an investigational drug;
- D. Changing the original target population to include a more at-risk population (example: previous exclusion for those with renal failure are now allowed to enroll, adding children or pregnant women to the study.);
- E. Adding additional procedures where the risk of the additional procedure is greater than the minimal risk;
- F. Adding a blood draw such that the total amount of blood drawn or frequency of blood draws exceeds what is considered expeditable; [45 CFR 46.402(a)].
- G. Adding an element that may breach the confidentiality of the subject such as specimen banking or genetic testing;
- H. An increase >25% in the number of participants to be "treated" which affects the statistical plan for the study and
- I. Requesting surrogate assent for a full board study (i.e. additional x-rays, DEXA scans).

#### **4.10.6 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.

When studies are subject to continuing review and protocols are subject to full board review, the IRB after review may approve the study as submitted, table or defer the study due to insufficient information, require changes and approve the study after re-review by the Chair or designee of full board or deny approval due to substantive issues related to the study.

Studies that are approved by expedited review, the continuing review, if required by the reviewer at the time of the initial review, will be done by the chair or a committee member. **A progress report** instead of a continuing review will be used for studies approved using the expedited review unless at the time of initial or progress report

review the IRB is requiring an actual continuing review **(45 CFR 46 .109(e))**. Progress report is not applicable clinical and high risk studies.

In reviewing the research, the reviewers may exercise all of the authorities of the IRB. In circumstances where continuing reviews has reasons to elevating the risk to more than minimal risk, the study will be sent to full board review. The IRB Chair or the IRB member may approve the study as submitted. The reviewer may request changes to the study. When changes are made, the IRB Chair or IRB member my re-review and approve the study. For detailed information on continuing review, go to Article 4. 11 below.

#### **4.10.7 Reportable Events**

The investigator is required to report promptly to the IRB (within 10 days of becoming aware of the event) deaths, unanticipated problems, anticipated events, protocol deviations and non-compliance. Anticipated and unanticipated events whether serious or not, that are not related to the study procedure, drugs or device and serious adverse events not related to the research are NOT reportable to the IRB.

When reportable events are submitted through CIRB, the IRB in a convened meeting may acknowledge the report as submitted requiring no additional action, IRB may require actions to mitigate the issue and upon receiving the follow up report, the full board, Chair or a designee will re-review the report prior to issuing a determination letter. In some cases, the full board may require an external action by reporting the event to the FDA or OHRP. If the reportable event is serious, the IRB may suspend the study. When IRB suspends a study, all research activity such as study visits, data collections, data analysis and enrollment must stop except when the intervention is in the best interest of subject. PI is required to consult with the Chair when intervention with the subject is necessary when the research activity is suspended. Review of reportable event may be deferred and discussed at the next convened meeting due to insufficient information. In general minimal risk studies may not require reporting; however, if there are adverse events that is reportable under this guidance they must also be reported to the IRB.

Studies that are approved under expedited review requiring submission of annual progress report also require adverse events reporting as anticipated or unanticipated problem.

#### **4.10.8 Suspension/Termination**

##### **4.10.8.1 IRB authority suspend or terminate research**

The IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head.

Suspension is defined as an action taken by the convened IRB or the IRB Chair or the IRB Director to temporarily stop research activities. If studies are suspended by the Chair or IRB Director, they must be reported to the convened IRB. Terms and conditions of suspension are explicitly detailed in IRBs communication to the PI. Suspended protocols are considered active requiring continuing review. Modifications to suspended protocols must be reviewed by the convened IRB.

Termination is defined as an action taken by the IRB to stop permanently all approved research activities. Terminations means the study is closed and does not require continuing review. All terminations must be approved by the convened IRB if the study was initially approved by the full board.

The convened IRB 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. When study approval is suspended or terminated, the IRB will require the investigator to inform any subjects currently participating that the study has been suspended or terminated.

If follow-up of subjects for safety reasons is permitted and/or required by the convened IRB, the convened IRB 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.)

Suspension or termination of protocols approved by the IRB can also be issued by Institution's officials. Such actions can be made by the Institution's President, Vice President for Research, the Institutional Official, and School Deans. Such actions by Institution's 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 Institution's Grievance Policy. The PI must report any suspension or termination of the conduct of research by Institution's officials to the IRB. The IRB will then determine what further actions may be warranted.

#### **4.10.9 Continuity of Care for Research Participants**

After the IRB has decided to suspend or terminate a research project, the IRB may make recommendations to investigators regarding ongoing care and treatment of human subjects who had been participating in the research. In making these recommendations,

the IRB shall take into account, among other factors, the risk to subjects from withdrawal of any investigational drug, device, or other treatment with the investigational drug or device can be continued with administration by another physician; and the need for further medical supervision of the subject.

#### **4.10.10 Investigator Hold**

An investigator, or the sponsor may temporarily or permanently place a hold on the protocol to stop approved activities. This is not to be construed as a suspension. When the investigator or the sponsor places a hold on an approved study, the investigator must inform the IRB through modification/amendment why the study is placed on hold, what approved activities are put on hold, what actions will be taken to protect subjects who have enrolled in that study and what actions are taken to prevent immediate harm to subjects and such preventive actions or proposed changes must be first approved by the IRB. Upon reviewing the written notification, the IRB Chair/IRB Director will review the report and after consulting with the investigator(s) the IRB will determine whether additional procedures are necessary to protect the rights and welfare of participants. In addition, the IRB Chair/IRB Director in consultation with the investigator prepares a plan to inform currently enrolled participants of investigator hold. The investigator is responsible for injury to enrolled participants.

#### **4.10.11 Protecting Currently Enrolled Participants**

Before an administrative, sponsor 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:

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

#### **4.11 Continuing Review – Full board approvals**

The IRB shall conduct continuing reviews of all full-board approved research at intervals specifically set by the IRB with notice to the PI. This review, using progress reports shall take place at least once per year until the research is concluded or discontinued. All continuing reviews are done in the context of the life of the protocol from initial approval until the date of continuing review. The IRB may recommend appropriate changes to the protocol based on approved amendments and adverse events.

In order to enable investigators to submit continuing review forms on time, the IRB will send out electronic renewal reminders 90, 60 and 30 days prior to 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. The continuing review applications submitted electronically through CIRB must include the following:

1. An electronic completed application;
2. Most recent approved consent form;
3. A new consent form if changes are made (a modification is required)
4. The current version of active protocol (a modification is required if changes to the protocol is made) and
5. Any new research information (modification required).

Those continuing reviews subject to full board meetings, all IRB members will have the access to the continuing review application on the CIRB site. Members will receive a notification when continuing reviews are posted on the CIRB site. After completion of administrative review by IRB staff, the Chair/the IRB Director will assign a primary reviewer and the reviewer will review the whole history of the protocol from its initiation. In the meeting, the primary member will lead the discussion and review the protocol while completing the continuing review checklist provided in the CIRB database.

#### **4.11.1 Continuing Review Expedited Studies**

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

- A. Research eligible for expedited review in accordance with regulations at **45 CFR 46.110**;
- B. Research reviewed by the IRB in accordance with limited IRB review as described in Sec **45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8)**;
- C. Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
  - i. Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
  - ii. Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

In the case of expedited review, the members will have full access to the continuing review or progress report submission on the CIRB site. The reviewer(s) will complete the continuing review checklist or complete the progress report checklist to determine whether the protocol meets the criteria for expedited approval and also meets the regulatory requirements for expedited review.

Protocols approved by the full board are not eligible for expedited continuing review and approval. At the time of continuing review, if the risk is determined to be more than minimal risk, expedited review will not be permitted.

#### **4.11.2 Lapses in continuing review**



Regulations do not allow approval extension when protocols have expired. If the continuing review does not occur prior to the expiration date, ALL RESEARCH ACTIVITIES MUST STOP. Likewise, if the IRB determines at the time of initial review a continuing review is required for an expedited study, all research activities must stop on the day the study has expired.. In both cases, no further research can be conducted until the IRB has re-approved the project and validated the consent form, if applicable. On the date of expiration, the IRB will send an electronic communication to the Principal and coinvestigators that all research activities including data collection must stop. Research activities include but are not limited to recruitment and enrollment of subjects, collection of specimens, research on previously collected specimens, review of medical records or other health information, and the performance of research tests/procedures, treatment or follow-up on previously enrolled subjects. IRB will send a letter to the PI to confirm that research must not be continued when a protocol/stud has expired. If treatment and/or follow-up of subjects are necessary for subject safety and welfare, the IRB must be informed in writing immediately and the IRB will consider these requests on a case-by-case basis. Federal regulations require that the IRB consider only what is in the best interest of the subjects when determining whether continuation of previously enrolled subjects is appropriate while continuing review is in process.

In order to initiate the expired protocol, re-approval by the IRB must occur. If the investigator requests re-approval within 60 days post expiration date, the investigator must submit a required continuing review application with all of the required documents listed above (Article 4.11) and reasons for lapse. In such cases, the IRB may consider reviewing the continuing review application and provide approval. If the expiration date has past 60 days, the investigator must submit a brand new application.

If continuing review results in “required changes”, the investigator is not allowed to enroll new subjects or access medical records or collect data or collect biospecimens after the expiration date. After receiving the response from the investigator, the IRB (full board or expedited review) will re-review the submission and approve after completing the checklist.

If the investigator does not respond at all, the IRB will administratively close the study in a convened meeting while ensuring that participants enrolled in the study are not put at risk.

#### **4.12 Study Closure and Final Report**

Principal investigators have the responsibility of informing the IRB when a study has been completed. A study is considered to be open and active until the investigator has submitted an electronic version of the Final Report to the IRB. When Final Reports are submitted, an administrative review will be conducted by the IRB staff. IRB Chair/IRB Director will review the form and report the closure of study to the IRB.

Faculty advisors for student research have the obligation to ensure that a final report to close the study is electronically filed with the IRB in a timely fashion. If protocols are not closed (Expedited and Full Board), IRB has the authority to not to review any new protocols submitted by the investigator (who has not closed the study) until the study which has been completed but not closed (not submitted final report).

When a principal investigator terminates employment or other association with the Institution, he or she is obligated to submit a Final Report to the IRB or formally transfer the protocol to another principal investigator via a modification, which will be reviewed and approved by the IRB. A study may be closed when all of the following apply:

- A. All subject recruitment and enrollment is complete (i.e., no new subject recruitment or enrollment are ongoing);
- B. All subject specimens, records, data have been obtained (i.e., no further collection of data/information from or about living individuals will be obtained);
- C. No further contact with subjects is necessary (i.e., all interactions or interventions are complete and no further contact with enrolled subjects is necessary) and
- D. Analysis of subject identifiable data, records, specimens are complete (i.e., use or access to subject identifiable data is no longer necessary. Note: this includes review of source documents by study sponsors.

In very rare cases, the IRB may grant special permission for the departing individual to remain as principal investigator on the project at another institution. Such cases are reviewed on a case by case basis. Before final approval is granted, the Principal Investigator must:

- i. Complete, sign and submit the "Agreement between RowanSOM and Departing Faculty member" to his/her Department Chair. The Agreement must also be signed by the Senior Associate Dean for Research and the Dean. Once signed, the form must be submitted electronically through CIRB; and
- ii. A copy of the IRB approval from the transferring Institution must be submitted electronically through CIRB if the study is continuing.

#### **4.13 Reporting IRB Actions**

All IRB actions (approval, request for change, suspensions and terminations) will be communicated as soon as possible but no later than 10 working days to the investigator through an email that provides access to the letter on the CIRB database. Along with the approval letter a stamped copy of the consent form with dates of approval and any other document such as advertisement, survey instrument will be provided to the investigator. The approval letter will have the level or category of review, the approval date and the expiration date. Investigators must print the approval letter and stamped consent form and other stamped documents in their protocol files as part of record keeping. IRB reports and minutes of the meeting are stored in the CIRB database. Hard copies of agenda and minutes are also available

##### **4.13.1 IRB Communication with Institution's Officials**

All official IRB communications with the administrative officials of the Institution will be the responsibility of IRB Director.

#### **4.13.2 Communication of Non-Compliance with Regulatory Agencies and Institution**

IRB, acting through the institutional official or his designee, shall provide a written report to the OHRP at HHS (for NIH PHS funded research only) or to the FDA of any of the following:

- A. Any serious or continuing noncompliance on the part of investigators conducting human subjects research with any of the regulations in these Guidelines, any IRB requirements or any OHRP or FDA regulations;
- B. Any serious unanticipated injury to human subjects in a study without an independent Data Safety Monitoring Board;
- C. Any suspension or termination of a previously approved research project of ANY FDA-REGULATED OR FEDERALLY-SPONSORED studies; and
- D. Any changes to the Federal Wide Assurance (FWA).
- E. All noncompliance determined by the IRB will be reported to the Department Head, the dean of the college and the VP for research (**Appendix 9**).

#### **4.14 Resolution of Disputes**

- A. The IRB has authority to approve, disapprove or, if necessary, resolve any differences of opinion between the PI and the IRB. Problems arising from PI disagreement or non-compliance with conditions set forth by the IRB including matters of compliance with reporting requirements of the FDA, HHS, or other pertinent governmental agencies shall be investigated by an ad-hoc sub-committee of the IRB appointed by the chair. The recommendation of the ad-hoc subcommittee will be presented to the full committee for review. The IRB will refer to the Signatory official, Provost, Vice President of Research and the Dean, his/her designee all matters requiring further inquiry and investigation under the Institution's Policies.
- B. No officer or administrator of the Institution can approve a proposal that has been disapproved by the IRB. However, the IO, IRB Chair, IRB Director or HPA, Provost, Vice president for Research can for reasons of institutional policy stop a study approved by the IRB.
- C. A proposal that has been rejected by the IRB, such proposals may be modified to satisfy objections and then resubmitted for IRB reconsideration.
- D. If a PI disagrees with a decision or action of the IRB, the PI may request that the IRB reconsider its decision by submitting a written request to the chair of the IRB. The chair may appoint an ad-hoc committee to review the issues in question and report back to the full committee for action.

#### **4.15 Protocol Resubmission**

Unless unusual circumstances exist, PIs should resubmit a revised protocol and consent form within 60 days of the IRB's action disapproving, tabling or requesting revisions of the protocol under review. PIs should inform the IRB of any reason why this deadline

cannot be met. Otherwise the IRB will consider the protocol withdrawn after 60-days. Investigators may request an extension through CIRB.

#### **4.16 IRB Review Checklist**

Reviewers are required to complete checklists that are in conjunction with IRB application on CIRB. There are several checklists that reviewers must complete to approve a study. Unless appropriate checklists are complete, the system will not allow the reviewer to approve the study.

## ARTICLE 5 - CONSENT PROCEDURES AND CONSENT FORMS

### **5.1 Consent Procedures and Consent Forms (45 CFR 46.117 and 21CFR Part 50)**

Informed consent is one of the primary ethical requirements of research with human subjects, reflecting the basic principles of Belmont Report, Respect for Persons, Beneficence, and Justice. Information must be presented to enable persons to voluntarily decide whether or not to participate as a research subject. It is a fundamental mechanism to ensure respect for persons through provision of thoughtful consent for a voluntary act. The procedures used in obtaining informed consent should be designed to educate the subject population in terms that they can understand. Therefore, informed consent language and its documentation (especially explanation of the study's purpose, duration, experimental procedures, alternatives, risks, and benefits) must be written in "lay language", (i.e. understandable to the people being asked to participate). The written presentation of information is used to document the basis for consent and for the subjects' future reference. The consent document should be revised when deficiencies are noted or when additional information will improve the consent process.

For further guidance on consent requirements and process go to the following links: <https://www.fda.gov/RegulatoryInformation/Guidances/ucm404975.htm>. and <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/informed-consent/index.html>.

Informed consent should assure that prospective human subjects understand the nature of the research and can knowledgeable and voluntarily decide whether or not to participate. This assurance protects all parties, including the investigator and the Institution, who may otherwise face legal hazards.

The "Surrogate consent" of someone other than the subject is not the same as the subject's own consent. An acceptable substitute, when a subject is unable to give informed consent, is primarily governed by law of the state where the consent is signed or study is being conducted. Surrogate consent is permitted with certain limitation in the State of New Jersey when subjects are unable to give their own consent. The state law and the Institution's policy require surrogate (proxy) consent or permission from a legally authorized representative, or some individual who has been previously designated for healthcare proxy. Broad consent may be obtained in lieu of informal consent with respect to storage, maintenance, and secondary research uses identifiable private information and identifiable biospecimens for secondary research purposes.

**Guidelines for Parental permission, Assenting Minors on a research project and Assent Waiver for Children are provided in Article 6, Subpart D, Section 6.26.**

**Informed consent FAQs from the Office for Human Research Protections (HHS.gov) is provided in the following link: <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/informed-consent/index.html>.**

## 5.2 Tips on Informed Consent

The process of obtaining informed consent must comply with the requirements of OHRP and FDA (**Appendix 2 and 3**). The documentation of informed consent must comply with Federal regulations and university policies. These Federal regulations can be found at <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/informed-consent-tips/index.html>. The following suggestions may help in the development of an approach and proposed language by investigators for obtaining consent and its approval by IRBs.

- A. Informed consent is not just a form - Information must be presented in detail to enable persons to voluntarily decide whether or not to participate as a research subject. It is a fundamental mechanism to ensure respect for persons through provision of thoughtful consent for a voluntary act. The procedures used in obtaining informed consent should be designed to educate the subject population in terms that they can understand.
- B. Informed consent must begin with a concise and focused presentation of the key information that is most likely to affect a prospective subject or Legally Authorized Representative in understanding the reasons why one might or might not want to participate in the research. This must be presented in a form that facilitates comprehension and understandable to the people being asked to participate.
- C. Informed consent as a whole must present information in sufficient detail relating to the research and must be organized and presented in such a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one may or may not want to participate.
- D. No informed consent may include any exculpatory language through which the subject or the legally authorized representative is made to waive or appear to waive any of the subject's legal rights or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.
- E. Describe the overall experience that will be encountered - Explain the research activity, how it is experimental (e.g., a new drug, extra tests, separate research records, or nonstandard means of management, such as flipping a coin for random assignment or other design issues). Inform the human subjects of the reasonably foreseeable harms, discomforts, inconvenience and risks that are associated with the research activity. If additional risks are identified during the course of the research, the consent process and documentation will require revisions to inform subjects as they are re-contacted or newly contacted.
- F. Describe the benefits that subjects may reasonably expect to encounter - There may be none other than a sense of helping the public at large. If payment is given to defray the incurred expense for participation, it must not be coercive in amount or method of distribution.
- G. Describe any alternatives to participating in the research project - For example, in drug studies the medication(s) may be available through their family doctor or clinic without the need to volunteer for the research activity.

- H. The regulations insist that the subjects be told the extent to which their personally identifiable private information will be held in confidence - For example, some studies require disclosure of information to other parties. Some studies inherently are in need of a Certificate of Confidentiality which protects the investigator from involuntary release (e.g., subpoena) of the names or other identifying characteristics of research subjects. The IRB will determine the level of adequate requirements for confidentiality in light of its mandate to ensure minimization of risk and determination that the residual risks warrant involvement of subjects.
- I. If research-related injury (i.e. physical, psychological, social, financial, or otherwise) is possible in research that is more than minimal risk (see Appendix 3) an explanation must be given of whatever voluntary compensation and treatment will be provided - Note that the regulations do not limit injury to "physical injury". This is a common misinterpretation.
- J. The regulations prohibit waiving or appearing to waive any legal rights of subjects - Consent language must be carefully selected that deals with what the institution is voluntarily willing to do under circumstances, such as providing for compensation beyond the provision of immediate or therapeutic intervention in response to a research-related injury. In short, subjects should not be given the impression that they have agreed to and are without recourse to seek satisfaction beyond the institution's voluntarily chosen limits.
- K. The regulations provide for the identification of contact persons who would be knowledgeable to answer questions of subjects about the research, their rights as a research subject, and research-related injuries. These three areas must be explicitly stated and addressed in the consent process and documentation - A single person is not likely to be appropriate to answer questions in all areas. This is because of potential conflicts of interest or the appearance of such. Questions about the research are frequently best answered by the investigator(s). However, questions about the rights of research subjects or research-related injuries (where applicable) may best be referred to those not on the research team. These questions could be addressed to the IRB, an ombudsman, an ethics committee, or other informed administrative body. Therefore, each consent document can be expected to have at least two names with local telephone numbers for contacts to answer questions in these specified areas.
- L. The statement regarding voluntary participation and the right to withdraw at any time can be taken almost verbatim from the regulations - It is important not to overlook the need to point out that no penalty or loss of benefits will occur as a result of both not participating or withdrawing at any time. It is equally important to alert potential subjects to any foreseeable consequences to them should they unilaterally withdraw while dependent on some intervention to maintain normal function. Don't forget to ensure provision for appropriate additional requirements which concern consent. The IRB may impose additional requirements that are not specifically listed in the regulations to ensure that adequate information is presented in the consent document.

- M. Additional elements of informed consent. When appropriate, one or more of the following elements of information shall also be provided to each subject:
- a. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;
  - b. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;
  - c. Any additional costs to the subject that may result from participation in the research;
  - d. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;
  - e. 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; and
  - f. The approximate number of subjects involved in the study.

### 5.3 Consent Process

Informed consent is an ongoing process, not something the investigator hands out to the prospective subject at the time of consenting. Informed consent assures that prospective human subjects will understand the nature of the research and can knowledgeably and voluntarily decide whether or not to participate. This assurance protects all parties, both the subject, whose autonomy is respected, and the investigator. A primary ethical responsibility of the Principal Investigator is to ensure that potential participants have been provided with all the information they might reasonably need to know. Any research protocol utilizing human participants requires the informed consent of those participants. Potential participants have the right to know what they are being asked to do prior to voluntary participation, no matter what the nature of the protocol and no matter how innocuous it may seem. The procedure of advising potential participants and obtaining voluntary agreement is known as the informed consent process. The process includes:

- A. The consent document is to be used as a guide for the verbal explanation of the study;
- B. The consent document should be the basis for a meaningful exchange between the researcher and the participant;
- C. The participant's signature provides documentation of agreement to participate in a study, but is only one part of the consent process.

Regulations require that the PI must document **(45 CFR 46.117)** the informed consent of each subject on a consent form approved and stamped by the IRB. Each IRB approved document must be signed and dated by the investigator or persons designated in the consent form as authorized to obtain consent, the person obtaining the consent, and the subject or his/her legally authorized representative. The IRB will approve procedures for verbal, electronic or implied consent only under exceptional circumstances.



#### **5.4 Standard Operating Procedures for Informed Consent**

Respect for Persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied. The IRB may approve the following recruitment procedures for enrolling research participants in your project.

- A. PI will insure that informed consent is obtained from each subject prior to the start of his or her participation in a clinical or behavioral research study.
- B. Only an IRB approved and stamped consent form is to be used for consenting subjects. A copy of the consent form should be provided to the participant.
- C. Each consent form will contain the following:
  - a. Institution's Name;
  - b. Name of the Study;
  - c. Investigator's Name;
  - d. Subject's Name;
  - e. Location where study will be done;
  - f. Entity where research will be conducted;
  - g. Sequentially numbered pages;
  - h. Authorization for collecting Protected Health Information;
  - i. Space for subject's initials on each page;
  - j. Version number or version date of the current consent form noted in the footer;
  - k. IRB stamp on each page indicating the approval and expiration date;
  - l. A consent signature page for subject, investigator or other individuals.  
authorized by the IRB to obtain consent, and witness signature to sign;
- D. The process should eliminate possibility of coercion of undue influence and eliminate use of exculpatory language;
- E. The informed language should be understandable and written at or about 8<sup>th</sup> grade level using lay terms and in a language that is understandable to the subject;
- F. The PI, other designated investigators, study coordinators, or other persons authorized to obtain consent will review the consent form with potential study subjects;
- G. Potential subjects will be informed whether the study involves the use of experimental devices or drugs, what the long-term health-related implications are, and how subjects' quality of life may be affected;
- H. The potential subject will receive a copy of the informed consent to read. The coordinator or PI will review each aspect of the study and answer all questions;
- I. If the subject wishes to speak with the principal investigator before signing the consent, a meeting will be scheduled to have all questions answered prior to the subject's signing the document;

- J. If the subject chooses to take a blank consent home to reread or discuss with family members, personal physician, or an attorney, a copy of the consent will be provided;
- K. Consent forms must be signed and dated by the participants or their legal representatives or surrogate prior to beginning any study-related procedures;
- L. If a surrogate is providing consent for the subject, the surrogate must receive some education about their role, the cognitive, and health status of the research participant, as well as about the study in which the participant may be involved before their consent may be requested. The surrogate must be informed of the risks, benefits, and alternatives to research before they give consent for an individual to participate. Such training must be documented;
- M. Consent forms must be signed and dated by a witness (only when required by the IRB) and/or the investigator or other persons authorized to obtain consent as required by the IRB and the sponsor;
- N. Investigators may pre-screen research subjects as approved by the IRB by personal interview, telephone screen, or chart reviews to determine general eligibility for a study prior to the informed consent being signed;
- O. Prior to signing the consent form, the subject or surrogate will be asked to reply, in his or her own words, and without immediate reference to the consent form, to the following questions.
  - a. What is the purpose of this study?
  - b. What will be done?
  - c. What risks and discomforts may occur from participating in this study?
  - d. What benefits may the subjects gain from participating in this study?
  - e. Ask the subjects to repeat in their own words about the goal of the research study. What will happen to them if they agree to be in the research study?
  - f. What do they expect to gain by participating in the study?
  - g. Tell them what will happen if they do not wish to participate in the study.
  - h. Tell them what will happen if they change their mind not to participate once the study has started.
  - i. Do the participants have any questions to ask back to you?
- P. Inform the prospective subject that they can take the consent form home have it read by others before they give consent;
- Q. Advise them to keep a copy of the consent form and the information to contact the researcher in a safe place in case they have to contact the researcher;
- R. A subject may participate in a study only if his/her answers demonstrate an informed understanding;
- S. If a protocol involves major risks; the IRB may require that subjects or the surrogate must be briefed twice with at least two (2) days between briefings. If it is anticipated that the second briefing may have to be waived in some circumstances, the PI should include such information at the time of initial review;
- T. All research subjects will be asked to initial every page of the informed consent to document that all pages were presented during the informed consent discussion;

- U. For clinical trials, the investigator will maintain an informed consent documentation sheet in the study binder indicating the name of the study, and the time and date of informed consent signed and when the IRB approval will expire and
- V. The investigator MUST maintain a copy of the signed consent form with the study specific regulatory binder, or as an appendix, in a secure location readily accessible to the investigator and that must be included in the initial protocol or at the time of modification.

### 5.5 General Requirements for Informed Consent

General requirements for informed consent, whether written or oral, are set forth in this paragraph and apply to consent obtained in accordance with the requirements set forth in **45 CFR 46.116 (b), (c) and (d)** See Article 5.6 below with basic elements of informed consent.

Broad consent may be obtained in lieu of informed consent obtained in accordance with Article 5.8 of this section only with respect to the storage, maintenance, and secondary research uses of identifiable private information and identifiable biospecimens.

Waiver or alteration of consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials is described in paragraph (e) of this section. General waiver or alteration of informed consent is described in Article 5.9 of this section. Except as provided elsewhere in this policy.

- A. Before involving a human subject in research covered by this policy, an investigator shall obtain the legally effective informed consent of the subject or the subject's legally authorized representative **(45 CFR 46.116 (a) (1))**.
- B. An investigator shall seek informed consent only under circumstances that provide the prospective subject or the legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence **(45 CFR 46.116 (a) (2))**.
- C. The information that is given to the subject or the legally authorized representative shall be in language understandable to the subject or the legally authorized representative **(45 CFR 46.116 (a) (3))**.
- D. The prospective subject or the legally authorized representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information **(45 CFR 46.116 (a) (4))**.
- E. Except for broad consent obtained in accordance with paragraph (d) of this section **(45 CFR 46.116 (a) (5))**:

- i. Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension **(45 CFR 46.116 (a) (5) (i))**.
  - ii. Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate **(45 CFR 46.116 (a) (5) (ii))**.
- F. No informed consent may include any exculpatory language through which the subject or the legally authorized representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence **(45 CFR 46.116 (a) (6))**.

#### **5.6 Basic Elements of Consent Form [45 CFR 46 116 (b)]**

- A. A statement that the study involves research. 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 that are experimental.
- B. A description of any reasonably foreseeable risks or discomforts to the subject.
- C. A description of any benefits to the subject or to others that may reasonably be expected from the research.
- D. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
- E. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
- F. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
- G. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
- H. 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. One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

- i. A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from subject or the legally authorized representative, if this might be a possibility; or
- ii. A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

### **5.7 Additional Elements of Informed Consent [45 CFR 46.116 (c)]**

Except as provided in paragraphs pertaining to elements of broad consent (see section 5.8 below), waiver or alteration of consent in research (see section 9.1 below) general waiver or e) or alteration of consent (see section 9.3 below) (f) of this section.

- A. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable.
- B. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's or the legally authorized representative's consent.
- C. Any additional costs to the subject that may result from participation in the research.
- D. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
- E. A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subjects.
- F. The approximate number of subjects involved in the study.
- G. A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit.
- H. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions.
- I. For research involving biospecimens, whether the research will (if known) or might include whole genome sequences (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or the exome sequence of that specimen).

### **5.8 Elements of Broad Consent**

**The IRB has made a decision not to use the Broad Consent. Regular adult and parental consent form must be used whenever identifiable biospecimens are going to be collected, stored or used for secondary research purposes.**

Elements of broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens. Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens collected for either research studies other than the proposed research or non-research purposes) is permitted as an alternative to the informed consent requirements as mentioned in 5.7 B and above. If the subject or the legally authorized representative is asked to provide broad consent, the following shall be provided to each subject or the subject's legally authorized representative.

- A. A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted;
- B. A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens.
- C. A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite).
- D. Unless the subject or legally authorized representative will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies.
- E. Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject; and
- H. An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm.

#### **5.9 Waiver of Alteration of Consent in Research Involving Public Benefit and service programs conducted by or subject to the approval of state or local officials**

- A. Waiver:** The IRB may waive the requirement to obtain informed consent provided the IRB satisfies the requirements of Article 5.10 C of this section.  
If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements of this section (elements of broad consent), and refused to consent, an IRB cannot waive consent for the

storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

- B. Alteration:** An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of informed consent set forth in Articles 5.6 and 5.7 (basic and additional elements) of this section provided the IRB satisfies the requirements of this section (requirements for waiver and alteration). An IRB may not omit or alter any of the requirements described in Article 5.5 of this section. If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under Article 5.8 of this section.
- C. Requirements for Waiver and Alteration: In order for an IRB to waive or alter consent as described in this subsection, the IRB must find and document that:**
- (i) 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:
    - 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; and
  - (ii) The research could not practicably be carried out without the waiver or alteration.

#### **5.10 General Waiver or Alteration of Consent [45 CFR 46.116 (f)]**

- A. Waiver:** An IRB may waive the requirement to obtain informed consent for research under 5.9 and 5.10 of this section provided the IRB satisfies the requirements of requirements of waiver and alteration described in this section. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements in Section 5.8\* of this section, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.
- B. Alteration:** An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of informed consent set forth in Articles 5.9 and 5.7 of this section provided the IRB satisfies the requirements of Article 5.10 of this section (requirements for waiver and alteration). An IRB may not omit or alter any of the requirements described in this section. If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under this section.
- C. Requirements for waiver and alteration:** In order for an IRB to waive or alter consent as described in this subsection, the IRB must first find and document that:
- (i) The research involves no more than minimal risk to the subjects;
  - (ii) The research could not practicably be carried out without the requested waiver or alteration;

- (iii) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
- (iv) The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
- (v) Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

### 5.11 Documentation of Informed Consent

- A. Except as provided in paragraph “C” of this section informed consent shall be documented by the use of a written informed consent form approved by the IRB and signed (including in an electronic format) by the subject or the subject’s legally authorized representative. A written copy shall be given to the person signing the informed consent form **(45 CFR 46.117 (a))**.
- B. Except as provided in Article 5.7 of this section, the informed consent form maybe either of the following.
  - 1. A written informed consent form that meets the requirements of **45 CFR 46.116**. The investigator shall give either the subject or the subject’s legally authorized representative adequate opportunity to read the informed consent form before it is signed; alternatively, this form may be read to the subject or the subject’s legally authorized representative.
  - 2. A short form written informed consent form stating that the elements of informed consent required by **45 CFR 46.116** have been presented orally to the subject or the subject’s legally authorized representative, and that the key information required by **45 CFR 46.116** was presented first to the subject, before other information, if any, was provided, The IRB shall approve a written summary of what is to be said to the subject or the legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Only the short form itself is to be signed by the subject or the subject’s legally authorized representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A Copy of the summary shall be given to the subject or the subjects’ legally authorized representative, in addition to a copy of the short form.
- C. An IRB may waive **(45 CFR 46.117 (c) (1))** the requirement for the investigator to obtain a signed informed consent form for some or all subjects if it finds any of the following:
  - i. That the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject (or legally authorized representative) will be asked whether the subject wants



documentation linking the subject with the research, and the subject's wishes will govern **(45 CFR 46.117 (c) (1) (i))**;

- ii. That 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 **(45 CFR 46.117 (c) (1) (ii))**; or
- iii. If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained **[45 CFR 46.117 (c) (1) (iii)]**.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects or legally authorized representatives with a written statement regarding the research **(45 CFR 46.117 (c) (2))**.

### **5.12 Applications and Proposals Lacking Definite Plans for Involvement of Human Subjects**

Certain types of applications for grants, cooperative agreements, or contracts are submitted to Federal departments or agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. These include activities such as institutional type grants when selection of specific projects is the institution's responsibility; research training grants in which the activities involving subjects remain to be selected; and projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. Except for research waived under **45 CFR 46.101 (i)**, or exempted under **45 CFR 46.104**, no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in this policy, and certification submitted, by the institution, to the Federal department or agency component supporting the research.

### **5.13 Research Undertaken Without the Intention of Involving Human Subjects**

Except for research waived under **45 CFR 46.101 (i)** or exempted under **45 CFR 46.104**, in the event research is undertaken without the intention of involving human subjects, but it is later proposed to involve human subjects in the research, the research shall first be reviewed and approved by an IRB, as provided in this policy, a certification submitted by the institution to the Federal department or agency component supporting the research, and final approval given to the proposed change by the Federal department or agency component.

### **5.14 Evaluation and Disposition of Applications and Proposals for Research to be conducted or supported by a Federal Department or Agency**

The department or agency head will evaluate all applications and proposals involving human subjects submitted to the Federal department or agency through such officers and employees of the Federal department or agency and such experts and consultants as the

department or agency head determines to be appropriate. This evaluation will take into consideration the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained.

### **5.15 Screening Recruiting, or Determining Eligibility**

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

- A. The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or
- B. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

If the study involves the use of protected health information, for screening, the investigator must obtain permission from the privacy officer by completing a Preparatory to Research form for determining eligibility; **however, subjects cannot be enrolled without the IRB approval.**

### **5.16 Screening Tests Prior to Study Enrollment**

For some studies that fall under FDA regulations, the use of screening tests to assess whether prospective subjects are appropriate candidates for inclusion in studies is an appropriate pre-entry activity. While an investigator may discuss availability of studies and the possibility of entry into a study with a prospective subject without first obtaining consent, informed consent must be obtained prior to initiation of any clinical procedures that are performed solely for the purpose of determining eligibility for research, including withdrawal from medication (wash-out). When wash-out is done in anticipation of or in preparation for the research, it is part of the research.

Procedures that are to be performed as part of the practice of medicine and which would be done whether or not study entry was contemplated, such as for diagnosis or treatment of a disease or medical condition, may be performed and the results subsequently used for determining study eligibility without first obtaining consent. On the other hand, informed consent must be obtained prior to initiation of any clinical screening procedures that is performed solely for the purpose of determining eligibility for research. When a doctor-patient relationship exists, prospective subjects may not realize that clinical tests performed solely for determining eligibility for research enrollment are not required for their medical care. Physician-investigators should take extra care to clarify with their patient-subjects why certain tests are being conducted.

Clinical screening procedures for research eligibility are considered part of the subject selection and recruitment process and, therefore, require IRB oversight. If the screening qualifies as a minimal risk procedure [**21 CFR 56.102(i)**], the IRB may choose to use expedited review procedures [**21 CFR 56.110**]. The IRB should receive a written outline

of the screening procedure to be followed and how consent for screening will be obtained. The IRB may find it appropriate to limit the scope of the screening consent to a description of the screening tests and to the reasons for performing the tests including a brief summary description of the study in which they may be asked to participate. Unless the screening tests involve more than minimal risk or involve a procedure for which written consent is normally required outside the research context, the IRB may decide that prospective study subjects need not sign a consent document [21 CFR 56.109(c)]. If the screening indicates that the prospective subject is eligible, the informed consent procedures for the study, as approved by the IRB, would then be followed.

Certain clinical tests, such as HIV infection, may have State requirements regarding (1) the information that must be provided to the participant, (2) which organizations have access to the test results and (3) whether a positive result has to be reported to the health department. Prospective subjects should be informed of any such requirements and how an unfavorable test result could affect employment or insurance before the test is conducted. The IRB may wish to confirm that such tests are required by the protocol of the study.

#### **5.17 Posting Clinical Trial Consent Form on Federal Website**

- A. For each clinical trial conducted or supported by a Federal department or agency, one IRB approved informed consent form used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal Website that will be established as a repository for such informed consent forms.
- B. If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal Website (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.
- C. The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.
  1. Preemption: The informed consent requirements in this policy are not intended to preempt any applicable Federal, state, or local laws (including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe) that require additional information to be disclosed in order for informed consent to be legally effective.
  2. Emergency Medical Care: Nothing in this policy 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 (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe).

#### **5.18 Consenting Non-English Speaking Subjects**

The regulations pertaining to the protection of human subjects require that informed consent information for research must be presented in "language understandable to the subject," and, in most situations, that informed consent be documented in writing (**45 CFR 46.116, 45 CFR 46.117 and 21 CFR 50.20**). Regulations allow oral presentation of informed consent information, however, it must be done in conjunction with a short form of written consent document that states that the consent has been presented orally and there must be a written summary of what is orally presented. Likewise, FDA regulations (**21 CFR 50.25 and 21 CFR 50.27**) require that informed consent information be presented in a language understandable to the subject and in most situations, that informed consent be documented in writing.

A witness to the oral presentation is required and the subject must be given copies of the short form document and the summary. For studies that will need the consent translated into another language (subjects may insist), the standard operating procedure is to hold the translation until the IRB has approved the English language consent form. Once the IRB has approved the consent form, a foreign language consent form can then be prepared and the following needs to be resubmitted for final approval of the foreign language consent form.

- A. Original English version of the consent.
- B. Foreign language version of the consent.
- C. A back translation from the foreign language back to English.
- D. A letter or a memo indicating that this translation was done by a different translator than the one who did the original translation.
- E. A letter describing the qualifications (e.g., Spanish speaking native or Vietnamese speaking native) of each translator and date of translation.
- F. Points D and E above may be written in the same letter.

The reason for the back translation is to make sure that the foreign language version contains all of the key elements of the English version. It is proper to anticipate that the back translation may not match word to word, but it is IRB's responsibility to make sure that key elements of the original consent is not left out in the foreign translation.

When enrolling non-English speaking research subjects, investigators must have a plan to manage communications with the person during all phases of study participation. This includes study visits as well as possible phone calls (e.g., when subjects or family members request information about side effects, drug doses, general questions). This management plan should be described in the IRB application as part of the procedure used to obtain consent.

### **5.19 Unexpected Enrollment of a Non-English Speaking Subject**

Individuals who are unable to verbally comprehend spoken English or read and comprehend documents written in English are considered non-English speaking subjects. Since such subjects are unable to understand English, it makes it impossible for a prospective subject to meaningfully volunteer and make an informed decision about

participation in research. Such subjects may also require the assistance of an interpreter or translator to make an informed decision to participate in the study.

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. In such cases:

- A. Investigators should carefully consider the ethical and legal ramifications of enrolling subjects when a language barrier exists;
- B. 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;
- C. 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 oral consent. A short English version of the informed consent document translated into the language the subject understands can be used to obtain consent and witness. Such short forms must be submitted to the IRB, the Chair shall determine whether or not such forms can be used;
- D. If the study design explicitly targets the enrollment of non-English speaking subjects, investigators are required to provide a written translation of the IRB-approved consent form and other relevant study documents (e.g., assents, authorizations, questionnaires, dosing instructions) in a language understandable to those participants. It is highly recommended that the documents first be submitted to the IRB in English, and once approved, be sent to the translator. It may be very costly if documents are initially submitted to the IRB with the foreign translations and then changes are requested thus requiring another translation and
- E. An alternate to this could be the use of a "Short Form". Contact the IRB Office to receive instructions for the use of a Short Form. A translator may assist in describing the contents in the native language of the subject. A witness must attest to the adequacy and voluntariness of the consent **(21 CFR 50.27(b)(2))**.

### **5.20 Use of Interpreters in the Consent Process**

Unless the investigator is fluent in the prospective subject's language, an interpreter will be necessary to facilitate the conversation. Interpreter is preferably someone who is fluent in both English and the subject's language. The interpreter also facilitates the question and answer phase of the consent process between the potential subject and the researcher (if the researcher is not the interpreter).

### **5.21 Consenting Emancipated Minors for Research**

Emancipation is the way that minors can become fully independent from their parents and have adult rights before reaching the age of 18. They are eligible to provide consent for routine clinical care. In the state of NJ, emancipated minors CANNOT give consent for

research procedures. Only the parents of emancipated minors are permitted to give research consent.

### **5.22 Participants with Limited Capacity to Consent**

In the case of a subject age 18 or over whose capacity or competence to give consent is limited for any reason, such as a comatose subject or a mentally-compromised adult, a legal guardian may provide consent. Institution's IRBs will accept substituted (or surrogate) consent in certain human subject research trials. For purposes of this policy, persons with "diminished capacity" means individuals who are unconscious, comatose or otherwise incapable of giving informed consent, as determined by the investigator and another duly licensed and qualified physician not otherwise involved in the research.

In the state of NJ, the provisions of the act (**L.2007, c.316, 1, eff. Jan. 13, 2008**) applies to medical research on persons with cognitive impairments, lack of capacity, or serious physical or behavioral conditions and life threatening diseases that is approved and monitored by an IRB that holds assurance with OHRP and either:

- A. Offers the prospect of direct benefit to the individual subjects, provided that the IRB has determined the risk is justified by the anticipated benefits to the subject 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 or his guardian or authorized representative, as applicable, shall be presented with the choice of the recognized treatment and the research protocol
- B. Does not offer the prospect of direct benefit to the individual 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 nature cannot be conducted without the participation of decisionally incapacitated persons as subjects; and (3) involves no more than a minor increase over minimal risk.

### **5.23 Consenting Illiterate Subjects**

If research participants are cannot read or write, due to illiteracy, the consent material should be read to the subject in the presence of impartial witness who observes the consenting process. Sufficient time should be provided for the subject to ask questions and answered, to ensure complete comprehension. If the subject is capable of doing so, the subject will mark "X" at the signature line, the person obtaining the consent signs and dates the consent form, witness signs and dates the consent form with the proviso that the informed consent was duly and freely given. A signed copy is presented to the subject. The IRB may permit video/audio recording of the consent process as part of the documentation of consent.

### **5.24 Alternative Approaches of Consenting Visually and/or Hearing Impaired Subjects.**

Alternative approaches may include braille consent for blind subjects provided the subject is able to read braille and sign the consent. If the blind subject does not read braille, an

oral consent should be taken. Use of audio recording is acceptable in such cases. Likewise, for hearing-impaired subjects, a sign language may be used provided the subject understands the sign language. A sign language specialist who is fluent in ASL may be used in this process. For hearing-impaired subjects who cannot read or write, the process described in Article 5.22 and 5.23 can be used.

### **5.25 Obtaining consent by Telephone, Skype, Social Media, or Interaction with a Website**

Consent obtained by these methods must still comply with all regulatory requirements about the process, the consent elements, and documentation of consent unless the requirements are waived by the IRB.

When the study does not meet the criteria for waiving documentation of consent, the researcher may propose a consent documentation process as follows:

- A. The subject receives a copy of the consent form in advance. For example, it could be mailed, emailed, or posted on a website;
- B. The researcher obtains consent over the phone or Skype. For website or social media interactions, the website may provide the researcher's contact information so that the potential subject can contact the researcher to set up a discussion by some method (phone or other, but it must provide the opportunity for a real-time or near real-time discussion.) and
- C. If the subject agrees to participate, he/she signs the consent form and returns it to the researcher for the researcher's signature, before any research procedures begin.

#### **5.25.1 Electronic Consenting (eIC)**

The joint guidance provided by OHRP and FDA makes recommendations on the use of electronic systems and processes that may employ multiple electronic media to obtain informed consent for both HHS-regulated human subject research and FDA-regulated clinical investigations of medical products, including human drug and biological products, medical devices, and combinations thereof (<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/use-electronic-informed-consent-questions-and-answers/index.html>) FDA's requirements for electronic records/electronic signatures, informed consent, and IRBs are set forth in **21 CFR parts 11, 50, and 56**, respectively. HHS requirements regarding the protection of human subjects are set forth in **45 CFR part 46**. The information presented to the subject, processes used for obtaining informed consent, and documentation of the electronic informed consent (eIC) must meet the requirements of these and other applicable regulations.

If the study is conducted or supported by HHS and involves an FDA-regulated product, the study is subject to both **45 CFR part 46 and 21 CFR parts 50 and 56**, meaning that both sets of regulations must be followed. Where the regulations differ, the regulations that offer the greater protection to human subjects should be followed.

For the purposes of this guidance, electronic informed consent refers to the use of electronic systems and processes that may employ multiple electronic media, including text, graphics, audio, video, podcasts, passive and interactive Web sites, biological recognition devices, and card readers, to convey information related to the study and to obtain and document informed consent.

The eIC must contain all elements of informed consent required by HHS and/or FDA regulations (**45 CFR 46.116 and 21 CFR 50.25**). The information must be in language understandable to the potential subject or the subject's LAR and conveyed in a manner that minimizes the possibility of coercion or undue influence regarding the subject's decision to participate in a study (**45 CFR 46.116 and 21 CFR 50.20**). Understandable means that the information presented to subjects is in a language and at a level the subject can comprehend, including an explanation of scientific and medical terms. To ensure that the eIC is presented appropriately and that subjects will have enough time to dedicate to the eIC process, the subjects should be informed of approximately how long the process will take and what information will be presented to them. Any eIC should be easy to navigate, allowing the user to proceed forward or backward within the system and to stop and continue at a later time. Hyperlinks may be provided where helpful. The eIC may also incorporate electronic strategies to encourage subjects to access all of the consent material before documenting their consent.

Electronic informed consent may be used to either supplement or replace paper-based informed consent processes in order to best address the subject's needs throughout the course of the study. For example, some subjects may prefer one method over another. Other subjects may have difficulty navigating or using electronic systems because of, for example, a lack of familiarity with electronic systems, poor eyesight, or impaired motor skills. In such cases, the eIC process may not be appropriate for these subjects. Therefore, subjects should have the option to use paper-based or electronic informed consent methods completely or partially throughout the informed consent process. Moreover, in some circumstances, it may be appropriate for investigators or study personnel to assist subjects in using the eIC technology. For example, study personnel may help the subject navigate the consent by clicking on links for the subject.

The investigator is responsible for ensuring that legally effective informed consent is obtained before that subject takes part in the study (**45 CFR 46.116 and 21 CFR 50.20, 312.60, and 812.100**). If the investigator delegates this responsibility, the responsibility should be delegated to an individual qualified by education, training, and experience to perform this activity. Whether part or all of the eIC process takes place on-site or remotely, the responsibility for obtaining informed consent remains with the investigator and the study personnel to which responsibility has been appropriately delegated. The investigator cannot delegate authority to obtain informed consent to the electronic system.



The consent process may take place at the study site when both the investigator and subject are at the same location. Or it may take place remotely (e.g., at the subject's home or another convenient venue) where the subject reviews the consent document in the absence of the investigator. The eIC materials may be provided for both on-site and remote access.

If the entire process takes place at the study site, the study personnel can personally verify the subject's identification, review the eIC content, answer questions about the material, have follow-up discussions, and witness the signing of the eIC.

If any or all of the consent process takes place remotely and is not personally witnessed by study personnel, the electronic system must include a method to ensure that the person electronically signing the informed consent is the subject who will be participating in the research study or is the subject's **LAR [21 CFR 11.100(b)]**. Examples of various methods that could be used include verification of a state-issued identification or other identifying documents or use of personal questions, biometric methods, or visual methods

Sometimes it may not be possible or necessary for all types of research covered by 45 CFR part 46 to verify that the person signing the informed consent is the subject or the subject's LAR who will be participating in the research study. Investigators are guided to apply a risk-based approach to the consideration of subject identity. For example, social behavioral minimal risk research will not typically warrant such verification. In addition, informed consent may be waived for minimal risk research meeting the requirements at **45 CFR 46.116(d)**.

Whether the eIC is obtained from the subject on-site or remotely, the eIC process must provide sufficient opportunity for the subject to consider whether to participate in accordance with Common Rule or FDA regulations. The investigator should have methods in place to ensure that the eIC process allows subjects the opportunity to consider whether or not to participate and to ask questions. See appropriate guidance at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM436811.pdf>. This may be accomplished by in-person discussions with study personnel or through a combination of electronic messaging, telephone calls, video conferencing, or a live chat with a remotely located investigator or study personnel. When live chat or video conferencing is used during the eIC process, investigators and study personnel should remind subjects to conduct the eIC discussion in a private location to help ensure privacy and confidentiality.

Subjects should be given a description of how and when they will receive answers to their questions, and they must be provided information on how to contact an appropriate individual for pertinent questions about the research and their rights and whom to contact in the event that they sustain a research-related injury. To assist the subject in understanding the material, the eIC may use interactive electronic-based technology,

which may include diagrams, images, graphics, videos, and narration. The eIC should be appropriate for the intended audience, taking into consideration the subject's age, language, and comprehension level. When appropriate, the eIC must contain a statement that significant new findings developed during the course of the research that may affect to the subject's willingness to continue participation will be provided to the subject or the subject's legally authorized representative (LAR). If an update or amendment to an eIC is necessary and could affect the subject's willingness to continue participation in the study, the eIC process must provide sufficient opportunity for the subject to consider whether to continue participation. If the eIC is updated or amended, the subject should be given sufficient opportunity to ask questions about the amended contents. In such cases, the subject or the subject's LAR must sign the amended eIC before the subject continues in the study. OHRP and FDA regulations permit the flexibility of using electronic and paper informed consent methods independently or in combination throughout the course of the study.

For FDA-regulated clinical investigations, the electronic system that supports the eIC must be secure with restricted access (**21 CFR 11.10 and 11.30**) and should include methods to ensure confidentiality regarding the subject's identity, study participation, and personal information after informed consent has been obtained.

If the personal information held by the Institution as a covered entity, the requirement of HIPAA security and privacy breach will apply. Thus, it is necessary that the information kept in the electronic system is encrypted. For example, the subject's information within an electronic system must be encrypted, unless the entity documents why encryption is not reasonable and appropriate in their specific circumstances and implements a reasonable and appropriate equivalent measure.

HIPAA authorizations may be obtained electronically, provided that the signature of the subject (or the subject's personal representative) is a valid electronic signature under applicable laws and regulations. The HIPAA Privacy Rule requires that when a covered entity seeks an authorization from a subject (or a subject's personal representative), the covered entity must provide the individual with a copy of the signed authorization; this requirement also applies where a HIPAA authorization is obtained electronically

#### **5.25.2 Capturing Electronic Signatures to document eIC (OHRP)**

The procedure for eIC may include an electronic method **to capture the signature** of the subject or the subject's LAR. OHRP and FDA regulations permit the use of electronic signatures when written informed consent is required. OHRP permits electronic signatures if such signatures are legally valid within the jurisdiction where the research is to be conducted. A copy of the informed consent must be provided to the person signing the form unless the requirement for documentation of waiver of consent has been waived by the IRB.

#### **5.25.3 Capturing Electronic Signatures to document eIC (FDA)**

FDA considers electronic records, electronic signatures, and handwritten signatures executed to electronic records to be trustworthy, reliable, and generally equivalent to a handwritten signature executed on paper. In order to be considered equivalent to full handwritten signatures, electronic signatures must comply with all applicable requirements under **21 CFR part 11.10**. The electronic system must also capture and record the date that the subject or subject's LAR provides consent.

FDA regulations permit a wide variety of methods to create electronic signatures, including using computer-readable ID cards, biometrics (a method of verifying an individual's identity based on measurements of the individual's physical feature(s) or repeatable action(s) where those features and/or actions are both unique to that individual and measurable), digital signatures (electronic signature based upon cryptographic methods of originator authentication, computed by using a set of rules and a set of parameters such that the identity of the signer and the integrity of the data can be verified), and user name and password combinations. FDA does not mandate or specify any particular methods for electronic signatures, including any particular biometric method upon which an electronic signature may be based.

Electronic signatures based on biometrics must be designed to ensure that they cannot be used by anyone other than their genuine owners. Therefore, suitable biometrics should be uniquely identified with the individual and should not change with time. In addition, electronic signatures based upon biometrics are accepted provided they meet the following requirements:

- A. They must contain pertinent information associated with the signing;
- B. They are subject to the same controls as electronic records and must be included as part of any human readable form of the electronic; and
- C. They must be linked to their respective electronic records (**21 CFR 11.70**).

IRBs, Investigators and sponsors obligated to consider issues like how the electronic signature is created and whether the informed consent or permission document can be produced in hard copy for review by the subject upon request. IRBs, investigators, and sponsors may rely on a statement from the vendor of the electronic system used for obtaining the electronic signature that describes how the signature is created and that the system meets the relevant requirements contained in **21 CFR part 11**. A copy of the informed consent must be provided to the person signing the form. FDA recommends that a copy of the signed informed consent form that includes the date when the eIC was signed be provided to the subject.

In FDA related research require that an organization verify the identity of an individual before it establishes, assigns, certifies, or otherwise sanctions an individual's electronic signature or any element of such electronic signature. However, FDA regulations do not specify any particular method for verifying the identity of an individual and accepts many different methods such as using some form of official identification, such as a birth

certificate, passport or a driver's license or use a well-developed security question to identify the individual.

#### **5.25.4 Required eIC materials to be submitted for IRB review**

The investigator should submit to the IRB copies of all forms (electronic and paper forms) and informational materials, including any videos and Web-based presentations, which the subject will receive and view during the eIC process. The investigator must obtain IRB approval for any subsequent modifications to the study-related information, whether electronic or in hard copy. OHRP and FDA recommend that an investigator discuss plans for using eIC with the IRB before finalizing development of the eIC to ensure that the IRB agrees that such a format may be used for the applicable research for obtaining informed consent.

#### **5.25.5 IRB's responsibilities in the eIC process**

HHS and FDA regulations require that an IRB review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by the applicable regulations. IRB must ensure there is an adequate informed consent process that protects the rights and welfare of subjects participating in HHS-regulated research and FDA-regulated clinical investigations. Therefore, the IRB must review and approve the eIC and any amendments to the eIC that the subject will receive and view. The IRBs must maintain and retain copies of materials that have been reviewed in accordance with regulations.

The IRBs will review any optional questions or methods used to gauge subject comprehension of key study elements. The IRB should also review the usability of the eIC materials to ensure that they are easy to navigate. If the program uses hyperlinks to convey study-related information, IRB will review the contents to which subjects are referred in order to determine if the study-related information that has been supplied is accurate and appropriate. Because Web sites are often modified over time, IRBs shall maintain the version of the Web site information that contains the study-related information that the IRB reviews and approves, either electronically or as a hard copy.

There is additional information on eIC on the following link:

<https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM436811.pdf>.

### **5.26 Consenting/Assenting Minors**

Consenting minors to enroll in research studies is provided in detail in Article 6 under vulnerable population Subpart D.

#### **5.26.1 Use of Electronic Consenting (eIC) for pediatric studies – Common Rule requirements**

The eIC process can be used to obtain assent from pediatric subjects (when required) and parental permission from their parent(s) or guardian. The general requirements for

informed consent, apply to parental permission, in addition to the requirements for permission by parents or guardians and for assent by children. Therefore, parental permission may be obtained and documented using the same eIC procedures as would be used for informed consent.

Absent a waiver of the assent requirement, or a determination that assent is not necessary, the IRB must determine that there are adequate provisions for soliciting the assent of children when, in the IRB's judgment, the children are capable of providing assent. When approving an eIC assent process, an IRB should consider whether the capability of a child to assent may be affected by the method used to obtain and/or document child assent. For example, if assent would otherwise be required, the method used to obtain eIC assent should not impede the child's capability to provide assent. The language and presentation of information must be understandable to the child. In addition, when the IRB determines that assent is required, it must also determine whether and how assent must be documented.

#### **5.26.2 Use of eIC for pediatric studies – FDA-regulated Clinical Investigations**

Depending on the method of identity verification used to satisfy the electronic signatures in FDA-regulated clinical investigations, a child may lack the documentation necessary to verify their identity for the purposes of preventing fraudulent use of electronic signatures (e.g., driver's license) If so, depending on the clinical investigation, it may be reasonable for the parent to initially document the child's assent, which can then be verified when the investigator first sees the child.

#### **5.27 Consent Monitoring**

To ensure that the consent process is adequate, the IRB may periodically monitor the consent process especially when studies recruit vulnerable subjects, studies are high risk and innovative, studies are conducted by inexperienced investigator or when IRB has some concerns that consent process may not be proper or when IRB is monitoring a study "for cause" or "not for cause" purpose. In such cases, the IRB may appoint a member (s) to monitor the process. The monitoring results will be reported to the IRB. The actions of the IRB may include that the IRB is satisfied with the consent process that the monitoring is no longer required or IRB may recommend continued monitoring, training and education of the person consenting the subject.

#### **5.28 Special Consent Provisions for Certain Emergency Research**

- A. Under NJ law, it is difficult to comply with the FDA requirement that, if a research subject lacks the physiological or mental capacity to consent (e.g., is unconscious).
- B. Consent may be given only by a legally authorized representative such as a legal guardian, a surrogate decision maker named in an advanced directive.
- C. When a patient lacks capacity to consent, it is often not possible to obtain consent from a legally authorized representative quickly enough for the subject

- to participate in the research, because of the limited therapeutic window for the proposed intervention.
- D. Because of the potential impact of this requirement on investigators' ability to conduct research involving unconscious patients, both the FDA and NIH recently issued procedures under which the IRB may waive, for all subjects in a trial, the requirement for consent from a legally authorized representative under emergency circumstances.
  - E. The following Articles of the Guidelines outline the IRB's requirements before it can consider a request to waive consent; for more details see 61 Fed Reg 51498-51533, (October 2, 1996), especially the Article-by-Article discussion in the preamble.

### **5.29 Criteria for Waiver of Consent for Emergency Treatment for Research**

Under the regulations (**45 CFR 46.116(a) and (b) and 46.408**), all of these seven requirements (A-G) must be met:

- A. The research subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence is necessary to determine the safety and effectiveness of a particular intervention.
- B. Obtaining informed consent is not feasible for the following reasons:
  - a. Because of the subjects' medical condition;
  - b. The intervention being studied must be administered before consent by a legally authorized representative is feasible; and
  - c. Individuals likely to become eligible for participation in the study cannot be identified prospectively.
- C. Participation in the study holds out the prospect of direct benefit to subjects because:
  - a. They face a life-threatening situation that necessitates intervention.
  - b. Results from animal and other pre-clinical studies support the potential of a direct benefit to subjects.
  - c. The risks of the study are reasonable in relation to what is known about the potential subjects' medical condition, the risks and benefits of standard therapy (if any), and what is known about the proposed intervention's risks and benefits.
- D. The study cannot practicably be carried out without the waiver of consent.
- E. Unless no drug or device is involved (**21 CFR Part 50**), the study must be conducted under a separate Investigational New Drug (IND) or Investigational Device Exemption (IDE) application approved by the FDA, even if the drug or device has previously been approved for use or is already under study pursuant to an IND or IDE. Contents of an earlier IND or IDE application may be incorporated by reference in the separate one required when consent is to be waived. The investigator may act as sponsor of the IND or IDE if the manufacturer is unwilling to do so. The FDA guidelines for exceptions from informed consent requirements for emergency research is available on the following link:

<https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM249673.pdf>.

- F. In the protocol, the investigator must define the potential therapeutic window and commits to attempting to contact either a subject's legally authorized representative or a family member during that time, before proceeding without consent. If the surrogate objects, the subject cannot be enrolled. The investigator also commits to, as soon as possible after a subject's consent has been waived, informing the subject; his/her legally authorized representative, or a family member of the situation, offering to remove the subject from the trial if the individual objects. The regulations require a summary of efforts to contact legally authorized representatives and family members to be made available to the IRB in continuing review applications and at the conclusion of the trial.
- G. In the protocol, the investigator describes the consultation, disclosure and data monitoring steps to be taken, as discussed further below.

### **5.30 Review Procedures for Community Consent**

FDA Guidelines for IRB role for community consultation is posted on the following link: <https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM249673.pdf>.

- A. The IRB will consider protocols submitted under this Article of the Guidelines in two steps. The first step will be a review of the protocol for compliance with all requirements of these Guidelines, including the steps that the investigator proposes to accomplish the required community consultation and disclosure. These proposed activities cannot begin until the IRB has approved the first-phase review.
- B. In the second step, the IRB must re-review the protocol after the community consultation and disclosure activities have been completed and the results are reported in an addendum to the protocol. Note that the study cannot begin until the FDA has also approved the IND or IDE application, if one is required.

### **5.31 Community Consultation**

- A. The regulations require consultation "with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn." The discussion of the regulations gives the following examples of ways in which community consultation may be achieved: a public meeting, establishing a panel of community members, and enlisting as consultants to the committee members of the community from which the subjects will be drawn. In addition to the above, for research as to which a relevant advocacy group exists in the Philadelphia area (e.g., American Diabetes Association, American Heart Association), it will usually be important to seek that group's written views concerning the proposed research.
- B. The Summary Protocol or a supplement to it should outline what community consultation activities the investigator deems to be appropriate. Individual IRB members and staff of the research compliance are available to provide assistance

in developing such proposed activities. The IRB must consider the results of all community consultation contacts before it makes a final decision about waiving consent.

### **5.32 Tips for Community Consultation**

Investigators must identify communities within the geographic location where illness or condition increase the susceptibility or risk for being involved in the research. Leaders of such community willing to serve as intermediaries for continued communication about the study is an important consideration. The role of the community member on the IRB is an essential part of such consultation. Make sure that all of the materials that are going to be used in community consultation are provided to the IRB and reviewed and approved by the IRB. Community consultation should make every effort to reach out to limited-English proficient individuals who may be susceptible to becoming research subjects in the study. Plan several meetings with the affected group by reaching out to the group using all possible media and methods to engage the group. Investigator must attend such meetings to explain the plan to include the affected in a manner that is understandable to the group in lay terms and language the group would understand. Investigators must consider the option of taking the IRB chair or an IRB member to these group meetings. Likewise, IRB members may volunteer to participate in such meetings. Investigators must make sure that the feedback received from the group is discussed in the IRB meeting.

### **5.33 Community Consultation and Public Disclosure**

- A. The regulations require, prior to beginning the study, "public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn of plans for the investigation and its risks and expected benefits." Notices in newspapers that are read generally in the areas in which subjects are likely to live will normally accomplish this, including paid newspaper advertisements. Mailing of individual notices is another alternative, such as to members of organizations with which the investigator has consulted.
- B. Another public disclosure is required of findings at the end of the trial. The Office of Research Compliance will work with investigators individually to ensure that this requirement is met, by such means as another round of news releases and notices to community groups, which were originally consulted, and to individuals who attended a previous public meeting or responded to previous disclosure activities.
- C. The investigator must provide a copy of each public disclosure to the sponsor of the study, who is required to forward them to the FDA.
- D. Ensure that a website and telephone number are included on all public disclosure materials.
- E. Develop a plan and submit such plans for public disclosure when the study is in progress and when the study is complete.

### **5.34 Data Safety Monitoring Committee**



The regulations require that a data monitoring committee (DSMB/DSMC) be established for all trials in which consent is waived. For multi-center trials, the drug or device manufacturer or other sponsor will typically name this committee. For the Institution's internally-initiated research projects involving terminally-ill participants, sponsored trials and NIH-sponsored clinical trials conducted at the Institution's or affiliated facilities, the investigator must propose in the protocol how this committee is to be constituted and its functions are. Information on how to set up a data safety monitoring committee is posted on the IRB website at <https://sites.rowan.edu/officeofresearch/compliance/irb/index.html>.

The IRB office will assist the investigator(s) in meeting this requirement, but it is up to the investigator to appoint members to DSMB/DSMC. Reports of DSMB/DSMC must be submitted electronically through CIRB by creating a Reportable Event, select "DSMB/DSMC Report". The Report must be made by the Chair or his/her designee of the DSMB/DSMC.

NIH Policy on for Data and Safety Monitoring is posted on the following link: <https://www.nidcr.nih.gov/Research/ToolsforResearchers/Toolkit/DSMBGuidelines.htm>. The guidance for data safety monitoring for clinical trials is available on the following link: <https://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127073.pdf>.

### **5.35 Costs of Fulfilling Requirements**

For a multi-center trial of a new drug or device, the manufacturer may be of assistance in providing suggested language for disclosure notices and by financial support for community consultation and disclosure activities. For a locally sponsored study, the investigator may be able to obtain a copy of the manufacturer's approved IND or IDE application through commercial sources (e.g., on-line data-bases) for such documents, if the manufacturer is unwilling to provide one. Investigators should consider the cost of these activities when preparing clinical trial and grant application budgets.

### **5.36 Special Reporting Requirement for studies in which the consent requirement has been waived**

In such cases, the investigator must:

- A. Document the efforts made to contact legally authorized representatives and family members, before beginning the intervention on the basis of waived consent.
- B. Include a report of such efforts in each request for continuing review.

### **5.37 Notification of Other (outside) IRB Actions**

If the IRB disapproves any request for waiver of consent, it will inform the investigator and sponsor in writing of its reasons for that action, and the sponsor is required to furnish copies of that notification to all other institutional review boards, which have considered the protocol, and to the FDA.

### **5.38 CIRB Consent Templates**

IRB Consent form Templates are posted on the following website:

<https://sites.rowan.edu/officeofresearch/compliance/irb/submissions/consenttemplates/index.html>.

- A. Adult consent form template (latest version).
- B. Assent form.
- C. Boilerplate consent for identifiable private information and identifiable biospecimens.
- D. Short Form – English version.
- E. Surrogate consent.
- F. Humanitarian Device Exemption (HDE) Consent.
- G. Audio/video tape addendum to consent form template.
- H. Short Form Consent in alternate languages.
- I. Template letter for participants.



**ARTICLE 6 - SPECIAL PROCEDURES FOR VULNERABLE SUBJECT POPULATIONS**  
**This Article covers Subpart B, C and D of the Common Rule and Subpart D of FDA regulations**

The federal regulations require that IRBs give special consideration to protecting the welfare of particularly vulnerable subjects, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. For research to which the HHS regulations are applicable, the HHS regulations set forth specific provisions on research involving fetuses, pregnant women, and human in vitro fertilization [45 CFR 46 Subpart B]; prisoners [45 CFR 46 Subpart C]; and children [45 CFR 46 Subpart D]. In general, these special regulations allow IRBs to approve research that is of minimal risk or that will benefit the subjects directly. Investigations involving these subjects that present significantly greater than minimal risk without direct benefit to them must be reviewed and approved by the Secretary of Health and Human Services, in consultation with appropriate experts.

FDA regulations [21 CFR.56.111(b)] states that when some or all of the subjects, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects. In order to approve research in which some or all of the subjects are children, an IRB must determine that all research is in compliance with part 50, subpart D of this chapter. Details about certain groups are presented below and a video is available from HSS to provide an overview.

([http://www.youtube.com/watch?v=SqRw6FevuXg&feature=player\\_embedded](http://www.youtube.com/watch?v=SqRw6FevuXg&feature=player_embedded).)

Such vulnerable population may include the following:

- Children, Minors
- Decisionally Impaired Persons
- Elderly and Aged Persons
- International Research Subjects
- Minorities (including Women)
- Pregnant Women, Fetuses, and Neonates
- Prisoners
- Students and Employees
- Terminally Ill Patients
- Traumatized and Comatose Patients

**6.0 Subpart B. Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research.** (<https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#subpartb>.)

The provisions of 45 CFR 46.201 – 207 are applicable to this subpart.

**6.1 Applicability (45 CFR 46.201)**

- A. The provisions of Subpart B apply to all HHS and Non-HHS-funded research.
- B. The provisions of Article 7 of these Guidelines apply to all research, development and related activities involving a pregnant woman, fetuses, and neonates of uncertain viability or non-viable neonates.
- C. Research conducted must also be in compliance with any applicable federal, state or local laws concerning fetuses, pregnant women and human in-vitro fertilization.
- D. Each of the exemptions are applicable to research subject to this subpart B if the conditions of the exemptions are met.

### **6.2 Definitions (45 CFR 46.201)**

The provisions of 45 CFR 46.102 shall be applicable to this subpart.

- A. "Dead fetus" means a fetus ex-utero that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord (if still attached).
- B. "Delivery" means complete separation of the fetus from the woman by expulsion or extraction or any other means.
- C. "Fetus" means the product of conception from implantation.
- D. "Neonate" means newborn.
- E. "Nonviable Neonate" means neonate after delivery that, although living, is not viable.
- F. "Pregnancy" encompasses the period of time from confirmation of 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.
- G. "Viable" as it pertains to the neonate, being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heart beat and respiration. The Secretary of Health may from time to time, taking into consideration medical advances, publish in a FEDERAL REGISTER, guidelines to assist in determining whether a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of subparts A and D.

### **6.3 Additional IRB Responsibilities (45 CFR 46.203)**

- A. In addition to other responsibilities defined in this part, the IRB shall review research covered by these guidelines (as prescribed by 45 CFR 46, Subpart B), to satisfy the conditions of all applicable sections of this subpart B or
- B. Determine that adequate consideration has been given to the manner in which potential subjects will be selected;
- C. Adequate provision has been made by the PI for monitoring the actual informed consent process.
- D. This monitoring may occur through a variety of mechanisms, including, when appropriate, participation by the IRB or subject advocates in:
  - a. Overseeing the actual process by which individual consents are secured (either by approving induction of each individual into the activity or

- verifying, perhaps through sampling, that approved procedures for induction or individuals into the activity are being followed) and
- b. Monitor the progress of the research activity and intervening as necessary through such steps as visits to the activity site and continuing evaluation to determine if any unanticipated risks have arisen.

#### **6.4. Research Involving Pregnant Women or Fetuses (45 CFR 46.204)**

Investigators conducting research with fetuses, pregnant women, and human in-vitro fertilization should know that the applicable federal regulations are summarized in **45 CFR §46.204**.

- A. When scientifically appropriate, preclinical studies, including studies in 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;
- B. 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;
- C. Any risk is the least possible for achieving the objectives of the research;
- D. 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, her consent is obtained in accord with the informed consent provisions of Article 5 of this Guidance.
- E. Each individual providing consent under paragraph D and E of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- F. 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 informed consent provisions of subpart A of this part, 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.
- G. For children as defined in **§45 CFR 46.402(a)** who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part;
- H. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- I. 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

- J. Individuals engaged in the research will have no part in determining the viability of a neonate.

**6.5. Research Involving Neonates (45 CFR 46.205)**

- A. Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:
  - a. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
  - b. Each individual providing consent under paragraph (2)(b) or (c)(v) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
  - c. Individuals engaged in the research will have no part in determining the viability of a neonate.
  - d. The requirements of paragraph (b) or (c) of this section have been met as applicable.
- B. 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:
  - a. The IRB determines that:
    - (i) 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
    - (ii) 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
  - b. 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 subpart A of this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.
  - c. Nonviable neonates. After delivery nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met:
    - (i) Vital functions of the neonate will not be artificially maintained;
    - (ii) The research will not terminate the heartbeat or respiration of the neonate;
    - (iii) There will be no added risk to the neonate resulting from the research;
    - (iv) The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and

- (v) The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of this part, except that the waiver and alteration provisions of §46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), 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 (c)(5).
- d. 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 subparts A and D of this part.

**6.6. Research Involving After Delivery, the Placenta, the Dead Fetus or Fetal Material (45 CFR 46.206)**

- A. Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.
- B. If information associated with material described in paragraph A of 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 subparts of this part are applicable.

**6.7 Research not Otherwise Approvable Which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Pregnant Women, Fetuses, or Neonates (45 CFR 46.207).**

The Secretary will conduct or fund research that the IRB does not believe meets the requirements of Section B or Section C above only if:

- A. 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
- B. The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the FEDERAL REGISTER, has determined either:
  - a. That the research in fact satisfies the conditions of 45 CFR 46.204 (Research involving pregnant women or fetuses), as applicable; or
  - b. The following:



- (i) 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;
- (ii) The research will be conducted in accord with sound ethical principles and
- (iii) Informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of this part.

### **SUBPART C: PROTECTIONS PERTAINING TO BIOMEDICAL AND BEHAVIORAL RESEARCH INVOLVING PRISONERS AS SUBJECTS**

Additional protections pertaining to biomedical and behavioral research involving prisoners as subjects are described in the following link:

<https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#subpartc>. The following website:

<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq> provides prisoner research FAQs and regulatory considerations for research involving prisoners.

#### **6.8 Applicability (45 CFR 46.301)**

- A. The provisions pertaining to review of research procedures specified in Article 7 of this guidance apply to all behavioral and biomedical research involving prisoners as subjects irrespective of funding source.
- B. Investigators conducting research with prisoners should familiarize themselves with the applicable laws in the jurisdiction where the prisoners are located. The provisions of Article 7.3 shall not be construed to authorize specific research involving prisoners as subjects. Investigators should be aware that research involving prisoners as subjects may be limited or prohibited by federal, state or local law. **Please note** that prisoners may be under constraints because of their incarceration which could affect their ability to make a timely voluntary and uncoerced decision whether or not to participate as subjects in a research project. Therefore, additional safeguards are needed to protect prisoners.
- C. The requirements of this subpart are in addition to those imposed under the other subparts of this part **(45 CFR 46.301)**.

#### **6.9 Purpose and Definitions (45 CFR 46.302 and 303)**

Inasmuch as prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research, it is the purpose of this subpart to provide additional safeguards for the protection of prisoners involved in activities to which this subpart is applicable.

- A. "Prisoner" means 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.

- B. "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.

### **6.10 IRB membership and Additional IRB Responsibilities (45 CFR 46.304 and 305)**

In addition to the responsibilities defined in **45 CFR 46.107 (IRB membership)**, the IRB shall, with respect to research covered by Article 6.0 of this guidance, undertake the following activities:

- A. IRB membership shall be modified as necessary on an ad hoc basis so that:
- a. A majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved and or prisoners, apart from their membership on the IRB; and
  - b. At least one member of the IRB shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity except that where a particular study is reviewed by more than one board only one board need satisfy this requirement.
  - c. The prisoner representative will review research involving prisoners and present the review at a convened meeting.
  - d. The prisoner representative must be present in the convened meeting when prisoner-related protocols are reviewed.
- B. The research under review represents one of the categories of research permissible under **45 CFR 46.306(a)(2)**;
- C. 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;
- D. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
- E. 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 Board 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;
- F. The information is presented in a language which is understandable to the subject population;
- G. Adequate assurance exists that parole boards 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

- H. Where the Board finds there may be a need for follow-up examination or care of participants 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 participants of this fact.
  - a. The Board shall carry out such other duties as may be assigned by the Secretary.
  - b. The institution shall certify to the Secretary, in such form and manner as the Secretary may require, that the duties of the Board under this section have been fulfilled.

IRB shall determine that: In addition to all other responsibilities prescribed for IRB, the IRB shall review research covered by this subpart and approve such research only if it finds that:

- A. The research under review represents one of the categories of research permissible under **45 CFR 46.305**
  - a. the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
  - b. prisons as institutional structures or prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
  - c. conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the FEDERAL REGISTER, of his/her intent to approve such research; or
  - d. practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of the intent to approve such research

#### **6.11 Permitted Research Involving Prisoners (45 CFR 46.306)**

- A. Biomedical or behavioral research conducted or supported by DHHS may involve prisoners as subjects only if:

- a. The institution responsible for the conduct of the research has certified to the Secretary that the Institutional Review Board has approved the research under **45 CFR 46.305** of this subpart; and
- b. In the judgment of the Secretary the proposed research involves solely the following:
  - i. 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;
  - ii. 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;
  - iii. Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction and sexual assaults) provided that the study may proceed only after the Secretary has consulted with appropriate experts including experts in penology medicine and ethics, and published notice, in the Federal Register, of his intent to approve such research; or
  - iv. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary has consulted with appropriate experts, including experts in penology medicine and ethics, and published notice, in the Federal Register, of his intent to approve such research.
- D. Except as provided in paragraph (a) of this section, biomedical or behavioral research conducted or supported by DHHS shall not involve prisoners as subjects.

### **6.12 Incarceration of Enrolled Subject**

If a subject becomes a prisoner after enrollment in a research study the investigator should notify the IRB immediately as a reportable event. Either the prisoner-subject must be withdrawn from study participation; or the IRB must, at the earliest opportunity, re-review the research protocol and consent form in accordance with the listed requirements. The IRB can either (a) approve the involvement of the prisoner-subject in the research or (b) determine that this subject must be withdrawn from the research. Note that if the subject-prisoner is withdrawn from study participation, he/she must be fully informed of the reason for such action or (c) wait until specific information becomes available prior to approving any interaction or intervention with or obtaining private information about, prisoners.

### **6.13 Waiver of Consent for Prisoners**

The HHS Secretarial waiver for certain epidemiological research conducted or supported by HHS functions as a fifth category of permissible research. The criteria for this category

are that the research must have as its sole purpose (i) to describe the prevalence or incidence of a disease by identifying all cases, or (ii) to study potential risk factor associations for a disease. The institution still must review the research under subpart C and certify to OHRP that an appropriately constituted IRB has reviewed the proposal and made all other required findings under HHS regulations at **45 CFR 46.305(a)** and receive OHRP authorization prior to initiating any research involving prisoners. All of the other requirements of subpart C apply to research in this category. However, even if informed consent is waived or altered, **subpart C of 45 CFR part 46** still requires that the subjects be clearly informed in advance that participation in the research will have no effect on their parole, if such notification is relevant. [**45 CFR 46.305(a)(6)**].

Note that prisoners cannot be involved in emergency research where the requirement for informed consent has been waived by the Secretary under the authority of 45 CFR 46.101(i).

#### **6.14 IRB Responsibilities (45 CFR 46. 304 - 305)**

The IRB shall prepare and maintain adequate documentation of IRB activities. For the purposes of subpart C, the IRB activities include making the specific findings and information required under HHS regulations at **45 CFR 46.305(a)**.

Some studies that involve interacting with prisoners may be reviewed through expedited review process when research presents no more than minimal risk. For research involving prisoners, the definition of minimal risk requires reference to physical or psychological harm, as opposed to harm or discomfort, to risks normally encountered in the daily lives, or routine medical, dental or psychological examination of healthy persons. Existing data such as prisoner record reviews are approved as expedited review. Such studies (minimal risk and records review) may be reviewed by non-prisoner representative. Continuing review procedures are similar to initial review procedures.

#### **6.15 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). The institution must send to OHRP a certification letter to this effect, which should also include the name and address of the institution and specifically identify the research protocol in question and any relevant HHS grant application or protocol. HHS conducted or supported research involving prisoners as subjects may not proceed until OHRP issues its approval in writing to the institution 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.

#### **6.16 Exemptions for Prisoner Research**

The exemptions at Section 4.1 above of these guidelines do not apply to research subject to this Subpart C, except for research aimed at involving a broader population that only incidentally become prisoners.

#### **6.17 Expedited Review for Prisoner Research**

In general all research involving prisoners must be reviewed by the convened IRB. If the research is reviewed under the expedited review procedure, the IRB member(s) reviewing the research must include a prisoner or prisoner representative.

For research involving prisoners, the regulations at **subpart C of 45 CFR part 46** define "minimal risk" as follows:

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 (**45 CFR 46.303(d)**).

The wording of the subpart C definition differs in several ways from the definition of "minimal risk" in subpart A of 45 CFR part 46, which applies generally to research involving human subjects. The differences are:

The subpart C definition refers to "physical or psychological harm" rather than "harm or discomfort" as in subpart A.

The subpart C definition compares the probability and magnitude of harm in the research to the probability and magnitude of those harms normally encountered in daily life, or in "routine medical, dental, or psychological examinations," rather than in daily life or "routine physical or psychological examinations or tests" as in subpart A.

The subpart C definition identifies "healthy persons" as the comparison group against which the risks of the research should be measured, rather than leaving the comparison group unspecified, as in subpart A. OHRP interprets the term "healthy persons" in this definition as referring to healthy persons who are not prisoners.

#### **6.18 Subject becoming Prisoner during the Course of Research or anticipated to becoming Prisoners**

Regulations do not have specific provisions for individuals on probation or parole. However, in such cases IRB may determine that these individuals are part of a vulnerable population and additional considerations should be taken when deciding to include these individuals in research. When submitting a protocol that includes individuals on

probation or parole the following documentation should be included with your submission. The documents are a letter of support from the subject's probation or parole officer and a statement in the informed consent document clearly indicating that their decision to participate in the research will have no impact on the individual's probation or parole.

If a human subject involved in ongoing research becomes a prisoner during the course of the study, and the relevant research proposal was not reviewed and approved by the IRB in accordance with the requirements for research involving prisoners under subpart C of 45 CFR part 46, the investigator must promptly notify the IRB. All research interactions and interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-subject must be suspended immediately, except as noted below. Upon receipt of the investigator's report that a previously enrolled research subject has become a prisoner, if the investigator wishes to have the prisoner subject continue to participate in the research, the IRB must promptly re-review the proposal in accordance with the requirements of subpart C, and the institution(s) engaged in the research involving the prisoner subject must send a certification to OHRP and wait for a letter of authorization in reply. Otherwise, the prisoner subject must stop participating in the research, except as noted below.

An important exception to the requirement that all research interactions or interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-subject must cease until the regulatory requirements for research involving prisoners are met. In special circumstances in which the investigator asserts that it is in the best interests of the subject to remain in the research study while incarcerated, the subject may continue to participate in the research until the requirements of subpart C are satisfied. The investigator must promptly notify the IRB of this occurrence, so that the IRB can re-review the study. Note that in these circumstances, some of the findings required by **45 CFR 46.305(a)** may not be applicable; for example, the finding required under **45 CFR 46.305(a)(4)** regarding the selection of subjects within the prison may not be applicable, if the subject was recruited outside of an incarcerated context. The IRB should document findings of non-applicability accordingly.

If investigators anticipate that some of the subjects in a planned research study population are likely to be prisoners or become prisoners during the course of the study (for example, subjects in substance abuse treatment studies) the IRB may review the research prospectively for prisoner involvement in accordance with the requirements of **subpart C of 45 CFR part 46**. When an IRB reviews a research proposal in which the subjects are not prisoners, but in anticipation of the likelihood that some of the subjects will become prisoners during the course of the research, some of the seven findings required by **45 CFR 46.305(a)** may not be applicable. As examples, if subjects are not recruited from within a prison, the finding under **45 CFR 46.305(a)(4)** would not be applicable; and, if there is no particular parole board involved yet, the finding under **45 CFR 46.305(a)(6)** would not be applicable. The IRB should document these findings

accordingly, and must certify the research to OHRP. The IRB must wait for OHRP to authorize the research study prior to initiating any interaction or intervention with, or obtaining identifiable private information about, prisoners.

#### **SUBPART D: Protections for Children Involved as Subjects in Research**

Additional Protections for Children Involved as Subjects in Research is described in the following link: <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#subpartd>. FAQ pertinent to research with children is available in the following link: <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/children-research/index.html>.

#### **6.19 Applicability (45 CFR 46.401)**

The provisions of Subpart D described below apply to all research involving children as subjects that is conducted or supported by the HHS.

#### **6.20 Definitions (45 CFR 46.402)**

- A. "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. Generally, the law considers any person under the age 18 to be a child.
- B. "Assent" means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.
- C. "Permission" means the agreement of parent(s) or guardian to the participation of their child or ward in research.
- D. "Parent" means a child's biological or adoptive parent.
- E. "Guardian" means an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.
- F. "Minimal Risk" means 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.

#### **6.21 HHS Regulations – Special Protections for Children**

When reviewing research with children as subjects, in addition to ensuring adherence to the general regulatory requirements of **45 CFR part 46, Subpart A and D**, the IRB shall consider the potential benefits, risks, and discomforts of the research to children and assess the justification for their inclusion in the research. In assessing the risks and potential benefits, the IRB should consider the circumstances of the children to be enrolled in the study—for example their health status, age, and ability to understand what is involved in the research—as well as potential benefits to subjects, other children with the same disease or condition, or society as a whole. If the research involves pregnant minors, then the requirements of Subpart B must be met. If research involves incarcerated minors then the requirements of Subpart C must be met.



For any protocol involving children, the IRB shall determine which of the four categories of research apply to that study, if any. OHRP recommends that the IRB document the rationale for this choice.

The HHS regulations at **45 CFR part 46, subpart D** permit IRBs to approve four categories of research involving children as subjects. For all four categories, the proposed research activity must meet the requirements for parental/guardian permission and child assent. Additional guidelines must be met in order for IRB to approve the proposed research activity.

**45 CFR 46.404- Research not involving greater than minimal risk to the children.**

To approve this category of research, the IRB must make the following determinations:

- a. The research presents no greater than minimal risk to the children; and
- b. Adequate provisions are made for soliciting the assent of the children when in the judgement of the IRB the children are capable of providing assent and the permission of their parents or guardians, as set forth in HHS regulations at 45 CFR 46.408.

**45 CFR 46.405- Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child subjects involved in the research.**

In order to approve under this category, the IRB must find that more than minimal risk to children is presented by an interaction or procedure that holds prospect of direct benefit for the individual subject by a monitoring procedure that is likely to contribute to the subject's well-being when IRB finds that:

- a. The risk is justified by the anticipated benefits to the subjects;
- b. The relation of the anticipated benefit to the risk presented by the study is at least as favorable to the subjects as that provided by available alternative approaches; and
- c. Adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in HHS regulations at **45 CFR 46.408**.

**45 CFR 46.406- Research involving greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research, but likely to yield generalizable knowledge about the subject's disorder or condition.**

In order to approve research in this category, the IRB must find that more than minimal risk to children presented by an intervention or procedure that does not hold prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute which is not likely to the well-being of the subject, only if the IRB finds:

The risk of the research represents a minor increase over minimal risk;

- a. The intervention or procedure presents experiences to the child subjects that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations;
- b. The intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition; and
- c. Adequate provisions are made for soliciting the assent when in IRB judgement children are capable of providing assent and the permission of their parents or guardians, as set forth in HHS regulations at 45 CFR 46.408.

A fourth category of research requires a special level of HHS review beyond that provided by the IRB.

**45 CFR 46.407- Research that the IRB believes does not meet the conditions of 45 CFR 46.404, 46.405, or 46.406 and research not otherwise approvable, which presents an opportunity to further understanding, prevention, or alleviate a serious problem affecting the health or welfare of children.**

If the IRB believes that the research does not meet the requirements of 45 CFR 46.404, 46.405, or 46.406, but finds that it presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children, it may refer the protocol to HHS for review. The research may proceed only if the Secretary, HHS, or his or her designee, after consulting with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following an opportunity for public review and comment, determines either: (1) that the research in fact satisfies the conditions of **45 CFR 46.404, 46.405, or 46.406**, or (2) the following

- a. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
- b. The research will be conducted in accordance with sound ethical principles; and
- c. Adequate provisions are made for soliciting the assent of children when in IRB judgement children are capable of providing assent and the permission of their parents or guardians, as set forth in HHS regulations at 45 CFR 46.408.

**6.22 Additional IRB Responsibilities (45 CFR 46.403)**

In addition to other responsibilities assigned to (see below) under this part, the IRB shall review research covered by this subpart (subpart D) and approve only research that satisfies the conditions of all applicable sections of this subpart.

- A. The IRB shall determine whether the research poses more than a minimal risk to the child subject. If less than minimal risk is posed, the IRB may approve the research pursuant to the relevant Articles of these Guidelines. The IRB will appropriately approve the study clearly indicating the risk level **45 CFR 46.404 or 405 or 406**. For further guidance on research involving children see Appendix 2.

- B. If the IRB finds that the research poses more than a minimal risk to the child; IRB must then determine whether the proposed intervention or procedure holds out the prospect of direct benefit for the individual child, or whether a proposed monitoring procedure is likely to contribute to the individual child's well-being.
  - a. If the IRB determines there is minimal risk, the research may be approved only if the IRB also establishes that:
    - i. The risk is justified by the anticipated benefit to the subjects;
    - ii. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
    - iii. Adequate provisions are made for soliciting the assent of the children, and permission of their parents or guardians as set forth in Article 6.25 and 6.27 of this guidance.
  - b. If the IRB determines there is more than minimal risk, then the research may only be approved if the IRB also establishes that:
    - a. The risk represents a minor increase over minimal risk;
    - b. 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;
    - c. The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition; and
    - d. Adequate provisions are made for soliciting assent of the children, and permission of their parents or guardians as set forth in Article 4.10 of these Guidelines.
- C. The IRB may approve research involving children that is not otherwise approvable only if:
  - 1. 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 children.
  - 2. The secretary of the DHHS, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either:
    - a. That the research in fact satisfied the conditions of **45 CFR §46.404-46.406 (Appendix 3)**, as applicable; or
    - b. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and the research will be conducted in accordance with sound ethical principles; and adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth in **45 CFR §46.408**.
- D. As provided herein, the IRB shall determine that adequate provisions are made for soliciting the assent of the children when, in the judgment of IRB, the children are capable of providing assent. In determining whether children are capable of

- assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular Protocol, or for each child, as the IRB deems appropriate. 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 where the IRB determines that the subjects are capable of assenting, the IRB may discuss and still waive the assent requirement under special circumstances depending upon the child's capacity or certain medical conditions in which child's assent may not be possible.
- E. The IRB shall determine, in accordance with and to the extent that consent is required by the Guidelines, that adequate provisions are made for soliciting the permission of each child's parent or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted. Where research is covered by Article 6) of these Guidelines and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
- F. In addition to the provisions for waiver contained in Article 6.26 of these Guidelines, if the IRB determines that a Research Protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status and condition. Permission by parents or guardians shall be documented in accordance with and to the extent required by these Guidelines. When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.
- G. The IRB may approve the use of children who are wards of the state or any other agency, institution or entity, in research covered by Article 6.23 of these Guidelines and approved under **45 CFR 46.406 or 45 CFR 46.407** only if such research is:
- a. Related to their status as wards; or Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.
  - b. If the research is approved under (G)(1,2) above, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any

other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

c. **Additional Safeguards for Children in Clinical Investigations Involving FDA-related Clinical Trials - 21 CFR Subpart D**

If the research involves the use of children in clinical trials involving investigational or off label use of approved drugs, biologicals or devices, the IRB shall determine the levels of risk and may approve the study pursuant to the relevant sections of these guidelines.

### **6.23 HHS Regulations for Wards**

The HHS regulations at **45 CFR part 46, subpart D** provide additional protections for children who are also wards of the State or any other agency, institution, or entity. These special protections for wards apply to two categories of research:

- A. Research approved by an IRB under **45 CFR 46.406**; or
- B. Research approved in accordance with the requirements of **45 CFR 46.407** that require a special level of HHS review beyond that provided by the Institutional Review Board (IRB).

As set out in **45 CFR 46.409**, before children who are wards of the State or any other agency, institution, or entity can be included in either of the two categories of research referenced above, the research must meet the following conditions:

- A. The research must be either related to the children's status as wards; or conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards; and
- B. The IRB must require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis.

One individual may serve as advocate for more than one child, and 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. The advocate should represent the individual child subject's interests throughout the child's participation in the research. The HHS regulations further require that the advocate not be associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

### **6.24 Appointment of Advocates to Oversee Child's Enrollment in Research**

HHS regulations at **45 CFR 46.409** require appointment of an advocate for each child who is a ward of the State or any other agency, institution, or entity, for the following two categories of research:

- A. Research approved by an Institutional Review Board (IRB) under **45 CFR 46.406**;  
or
- B. Research approved under **45 CFR 46.407** that requires a special level of HHS review beyond that provided by the IRB.

The advocate must be an individual who has the background and experience to act in, and agrees to act in the best interest of the child throughout the duration of child's participation in research. The added protection is intended to ensure that the ward, who is particularly vulnerable, is not exploited, coerced, or subjected to undue influence or harm in the course of research. The advocate is not associated with research, the researcher, or the guardian organization. The IRB has the right to review and approve the process for appointing advocates. Advocates could be a member of the IRB, representative from Rowan's health advocacy, or ombudsman's office, or a counsellor responsible for child's rights and welfare.

### **6.25 Parental Permission**

If investigators are recruiting children, they must obtain permission from parents before the recruitment process begins. In general, permission should be obtained from both parents before a child is enrolled in research. However, the Institutional Review Board (IRB) may find that the permission of one parent is sufficient for research to be conducted under **45 CFR 46.404 or 45 CFR 46.405**. When research is to be conducted under **45 CFR 46.406 and 407** permission must be obtained from both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. The basic elements of the permission form may not differ too much from the consent form, but includes additional elements to protect children from research related risks. The IRB will determine who will give the permission, but the IRB may determine that permission from one parent may be adequate. When parents are not available or deceased, a court appointed legal guardian may give permission. The legal guardian must provide evidence to the IRB that he/she has the decision-maker's status. Child advocates or caregiver, though they can give permission for standard of care treatment, they will be not permitted to provide permission for research. IRB also has the authority to waive the permission following the same conditions that are used for waiving consent for adults. IRB may grant waiver of permission for research involving no greater than minimal risk. In this case, IRB may require assent for the child. If the research involves greater than minimal risk, IRB will not grant permission waiver.

### **6.26 Parental or Guardian Permission Waiver**

The IRB may waive the requirements for obtaining parental or guardian permission if it makes and documents the findings under either **45 CFR 46.116(c) or (d)**.

In addition to the provisions for waiver contained in **45 CFR 46.116(c) and (d)**, if the IRB determines that a research protocol is designed to study conditions in children or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may

waive the parental permission requirements provided that an appropriate mechanism is in place to protect the children, and provided that the waiver is not inconsistent with federal, state, or local law **[45 CFR 46.408(c)]**. The choice of an appropriate substitute mechanism (for example, appointing a child advocate or an assent monitor) for protecting children participating in research would depend on the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and the child's age, maturity, status, and condition **[45 CFR 46.408(c)]**.

### **6.27 Child's Assent**

In most cases, the IRB may require permission from the parent and assent of the child (ages 7 and above). "Assent" means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent. **[45 CFR 46.402(b)]**.

This means 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 Institutional Review Board (IRB) is charged with taking into account the ages, maturity, and psychological state of the children involved. The IRB will 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 shall 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.

If the child is between the ages and 7 and 12, IRB may recommend oral assent along with providing the child with written information about research procedures, risks and benefit. Children above 13 years provide written assent at the 8<sup>th</sup> grade level. When assent is required, the child must agree to participate in research.

IRB may decide that the child's assent is not needed in certain circumstances. They include (1) when IRB determines that one or more of the children participating in the study are incapable of giving assent or (2) The research holds a prospect of direct benefit

and it is important for the health and welfare of the child and the intervention is only available as research or (3) The child does not have the capacity, due to age (under 7 years), maturity and psychological status to assent for the proposed research activity. Before the child reaches the age of 18, the child must be prepared to provide his/her own consent. When the child turns to 18, the child must be re-consented. Assents obtained from the children or assent waiver will be documented.

### **6.28 Child's Assent Waiver**

The Institutional Review Board (IRB) is responsible for deciding whether child assent is required in proposed research activities. The IRB should require child assent unless it can be appropriately waived, or if the child is not capable of providing assent.

The regulations at **45 CFR 46.408(a)** identify three types of circumstances where the IRB may determine that waiver of children's assent is appropriate.

- A. If the capability of some or all of the children is so limited that they cannot reasonably be consulted.
- B. If the intervention or procedure involved in the research holds out the prospect of direct benefit to the health or well-being of the children and is available only in the context of the research.
- C. If the research meets the same conditions as those for waiver or alteration of informed consent in research involving adults, as specified in the regulations at either **45 CFR 46.116(c)** or **45 CFR 46.116(d)**.

The IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. 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 where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances, in which consent may be waived in accord with **§46.116 of Subpart A**.

- D. When parents are giving permission, the IRB may find that the permission of one parent is sufficient for research to be conducted under **45 CFR 46.404** or **45 CFR 46.405**.
- E. Where research is covered by **45 CFR 46.406** and **45 CFR 46.407**, and permission is to be obtained from parents, both parents must give their permission, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
- F. If the IRB determines that a research protocol is designed for conditions or for a subject population, for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in Subpart A of this part and paragraph (b) of this section, provided an appropriate mechanism for protecting the children



who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with Federal, state or local law.

### **6.29 Disagreements between a Child and Parents**

If a child is capable of assent and the Institutional Review Board (IRB) requires that assent be sought, it must be obtained before the child can participate in the research activity. Thus, if the child dissents from participating in research, even if his or her parents or guardian have granted permission, the child's decision prevails.

However, the regulations at **45 CFR 46.408(a)** state that the IRB may waive the assent requirements if the intervention or procedure involved in the research holds out the prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of research. Conversely, if a child assents to participate in research, and parental permission has not been waived by the IRB, the permission of the parents or guardian is also required before the child can be enrolled in the research.

### **6.30 Order of Parental Permission or Child's Assent**

Regulations do not specify the order in which parental or guardian permission and child assent should be sought. Therefore, Institutional Review Boards (IRB) may determine the appropriate order given the research and the context in which it will be conducted.

In general, the IRB recommends that parental or guardian permission should be sought before seeking the assent of a child, particularly in more than minimal risk research, unless the requirement for obtaining parental or guardian permission can be waived. There might be some cases, however, involving minimal risk research, where it would be reasonable to seek child assent prior to seeking parental permission.

### **6.31 Guidelines when a Child Reaches the Age of Consent**

The Office for Human Research Protections (OHRP) notes that informed consent should be viewed as an ongoing process throughout the duration of a research project. When a child who was enrolled in research with parental or guardian permission subsequently reaches the legal age of consent to the procedures involved in ongoing research, the subject's participation in the research is no longer regulated by the requirements of 45 CFR part 46.408 regarding parental or guardian permission and subject assent.

Unless the Institutional Review Board (IRB) determines that the requirements for obtaining informed consent can be waived, the investigators should seek and obtain the legally effective informed consent, as described in **45 CFR 46.116**, for the now-adult subject for any ongoing interactions or interventions with the subjects. This is because the prior parental permission and child assent are not equivalent to legally effective informed consent for the now-adult subject. However, the IRB could approve a waiver of informed consent under **45 CFR 46.116(d)**, if the IRB finds and documents that the required conditions are met.

Similarly, if the research does not involve any ongoing interactions or interventions with the subjects, but continues to meet the regulatory definition of “human subjects research” (for example, it involves the continued analysis of specimens or data for which the subject’s identity is readily identifiable to the investigator(s)), then it would be necessary for the investigator(s) to seek and obtain the legally effective informed consent of the now-adult subjects. The IRB may consider, if appropriate, a waiver under 45 CFR 46.116(d) of the requirements for obtaining informed consent in order for the subjects to continue their participation in the research.

### **6.32 Child Giving Consent to Treatment without Parental Permission**

Children are defined as those who have not attained the legal age to consent to treatment or other procedures involved in research. However, if treatments or procedures are outside the research context (under applicable state and local laws, such as treatment to sexually transmittable disease (STD) or pregnancy such individuals would not meet the definition of children as defined at **45 CFR 46.402(a)**.

### **6.33 Exemptions for Research Involving Children**

The exemptions listed in Article 4.1 of these guidelines describes exemption categories permitted. Those exemptions listed in paragraphs **45 CFR 46.104 (d) (1), (4), (5), (6), (7) and (8)** included in Article 4.1 of these guidelines may be applied to research subject to Subpart D if the conditions of exemptions are met. Thus the only exemptions that are applicable to research involving children are:

- A. Research only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedure, interview procedures or observation of public behavior (including visual or auditory recording) of at least one of the following criteria is met:
- B. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
- C. Any disclosure of the human subjects’ responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation

However, the information obtained is recorded by the investigator in such a manner that the identity of the human subjects’ can readily be ascertained. Directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination.

If research involves this Exempt category 2 (iii), such research will be reviewed by an IRB member who is qualified to conduct such review and the review will be conducted as an expedited review.

The exemptions listed in Article 6.31 of these guidelines are not applicable for research that fall under the FDA regulations.

### **6.34 FDA Title 21 Section 50.50 - IRB duties Involving Children**

Additional safeguards for children in clinical investigations per FDA regulations is provided in the following link:

<https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50&showFR=1&subpartNode=21:1.0.1.1.20.4>.

In addition to other responsibilities assigned to IRBs under this part and part 21 CFR part 56 of this chapter, each IRB shall review clinical investigations involving children as subjects covered by this subpart D and approve only those clinical investigations that satisfy the criteria described in **50.51, 50.52, or 50.53** and the conditions of all other applicable sections of this subpart D.

#### **6.34.1 Clinical investigations not involving greater than minimal risk. (FDA Sec. 50.51)**

Any clinical investigation within the scope described in **50.1 and 56.101** of this chapter in which no greater than minimal risk to children is presented may involve children as subjects only if the IRB finds and documents that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians as set forth in **50.55**.

#### **6.34.2 Clinical investigations involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects (FDA Sec. 50.52)**

Any clinical investigation within the scope described in **50.1 and 56.101** of this chapter in which more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, may involve children as subjects only if the IRB finds and documents that:

- (a) The risk is justified by the anticipated benefit to the subjects;
- (b) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
- (c) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians as set forth in 50.55.

#### **6.34.3 Clinical investigations involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subjects' disorder or condition. (FDA Sec. 50.53)**

Any clinical investigation within the scope described in 50.1 and 56.101 of this chapter in which more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is not likely to contribute to the well-being of the subject, may involve children as subjects only if the IRB finds and documents that:

- (a) The risk represents a minor increase over minimal risk;

- (b) 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;
- (c) The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition that is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
- (d) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians as set forth in **50.55**.

**6.34.4 Clinical investigations not otherwise approvable that present an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (FDA Sec. 50.54)**

If an IRB does not believe that a clinical investigation within the scope described in **50.1** and **56.101** of this chapter and involving children as subjects meets the requirements of **50.51, 50.52, or 50.53**, the clinical investigation may proceed only if:

- (a) The IRB finds and documents that the clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and
- (b) The Commissioner of Food and Drugs, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, determines either:
  - (1) That the clinical investigation in fact satisfies the conditions of **50.51, 50.52, or 50.53**, as applicable, or
  - (2) That the following conditions are met:
    - (i) The clinical investigation presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
    - (ii) The clinical investigation will be conducted in accordance with sound ethical principles; and
    - (iii) Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians as set forth in **50.55**.

**6.34.5 Requirements for permission by parents or guardians and for assent by children (FDA Sec. 50.55)**

- (a) In addition to the determinations required under other applicable sections of this subpart D, the IRB must determine that adequate provisions are made for soliciting the assent of the children when in the judgment of the IRB the children are capable of providing assent.
- (b) In determining whether children are capable of providing assent, the IRB must take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in clinical investigations under a particular protocol, or for each child, as the IRB deems appropriate.

- (c) The assent of the children is not a necessary condition for proceeding with the clinical investigation if the IRB determines:
  - (1) That the capability of some or all of the children is so limited that they cannot reasonably be consulted, or
  - (2) That the intervention or procedure involved in the clinical investigation 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 clinical investigation.
- (d) Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement if it finds and documents that:
  - (1) The clinical investigation involves no more than minimal risk to the subjects;
  - (2) The waiver will not adversely affect the rights and welfare of the subjects;
  - (3) The clinical investigation could not practicably be carried out without the waiver; and
  - (4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.
- (e) In addition to the determinations required under other applicable sections of this subpart D, the IRB must determine that the permission of each child's parents or guardian is granted.
  - (1) Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient, if consistent with State law, for clinical investigations to be conducted under **50.51 or 50.52**.
  - (2) Where clinical investigations are covered by **50.53 or 50.54** and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child if consistent with State law.
- (f) Permission by parents or guardians must be documented in accordance with and to the extent required by **50.27**.
- (g) When the IRB determines that assent is required, it must also determine whether and how assent must be documented.

#### **6.34.6 Wards (FDA Sec. 50.56)**

- (a) Children who are wards of the State or any other agency, institution, or entity can be included in clinical investigations approved under 50.53 or 50.54 only if such clinical investigations are:
  - (1) Related to their status as wards; or
  - (2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.
- (b) If the clinical investigation is approved under paragraph (a) of this section, the IRB must require appointment of an advocate for each child who is a ward.
  - (1) The advocate will serve in addition to any other individual acting on behalf of the child as guardian or in loco parentis.
  - (2) One individual may serve as advocate for more than one child.

- (3) The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interest of the child for the duration of the child's participation in the clinical investigation.
- (4) The advocate must not be associated in any way (except in the role as advocate or member of the IRB) with the clinical investigation, the investigator(s), or the guardian organization.

## **6.35 Special Populations**

### **6.35.1 International Populations**

The review of foreign site research presents several challenges to the IRB. The IRB is required to have and document knowledge of the "local research context" and may require additional information from investigators before final approval of foreign site projects can be given. Information about local laws and customs, local IRBs, agencies, or "gatekeeper" organizations, and informed consent alternatives must usually be provided for international research. The FDA requires compliance with "the laws and regulations of the country in which the research is conducted."

Under the Institution's Assurance of compliance, federally funded projects that will recruit subjects through foreign institutions must provide formal assurance of compliance with federal regulations. Additional paperwork may be required by OHRP before Institution's IRBs can approve such projects.

### **6.35.2 Minorities (including women)**

Nevertheless, IRBs are required to include additional safeguards in studies where "some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as, economically or educationally disadvantaged persons" (**see 45 CFR 46.111(b)**).

The NIH guidelines concerning inclusion of women is "It is the policy of NIH that women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification establishes to the satisfaction of the relevant Institute/Center Director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research."

### **6.35.3 Students and Employees**

Any participation of students in research must be voluntary. Reasonable levels of extra credit or rewards may be offered for participating in research. If extra credit or rewards are offered for participation, students must be provided with and informed of non-research alternatives involving comparable time and effort to obtain the extra credit in order for the possibility of undue influence to be minimized. However, if participation in research is a course requirement, students must be informed of non-research alternatives involving comparable time and effort to fulfill those requirements in order for the possibility of undue influence to be minimized. Moreover, students must not be penalized for refusing to participate in research [**45 CFR 46.116(a)(8)**].

The Institution or Departments within the Institution may establish “student subject pool” to identify students who might be willing to participate in research, even when the exact nature of the research to be conducted has not yet been determined. No Institution’s department may establish a student subject pool without prior written authorization from the IRB Office. Extra credits or other rewards are often offered as an incentive to encourage participation. Students who sign up for such pools have not legally consented to participate in a research study since they have not been provided with sufficient information concerning the exact study in which they would participate. Thus, signing up to be in a subject pool is only a first and preliminary step by which individuals can indicate their willingness to be considered for research participation. The student must also provide informed consent, unless the consent requirement is waived by an IRB once he or she is being considered for a specific study **(45 CFR 46.116)**. Furthermore, individuals in the pool must be free to decline participation in any available research projects without penalty **[45 CFR 46.116(a)(8)]**.

When Institution’s students are enrolled in a course in which participation as human subjects becomes an integral part of the course, the official University course catalogue and timetable shall state that fact in the course description. A statement such as the following shall be included in the course description: "Includes limited voluntary participation as a subject in research activities." This statement will serve to alert registrants, but it does not suffice as the only means of ensuring that the subjects' participation in a specific research activity is voluntary.

Some college students are minors—when recruiting widely from a university population, especially one including freshmen, researchers should be clear on whether they will or won't exclude minors from the research study. If minors are not excluded, parental consent must be obtained.

Less direct recruitment practices (e.g., public sign-up sheets) are preferable to person-to-person invitations (especially those made by faculty to his/her-own students).

Payment in the form of course credit should not constitute a significant percentage of the total credit for the course. The investigator will be asked to provide the details about the course grading system when applying for approval of a credit-for-research agreement.

Appropriate segments of the following statement should be incorporated into consent forms for studies where students or employees will be deliberately targeted in the research population: "Participation in this research is voluntary. Your decision to participate, decline, or withdraw from participation will have no effect on your grades at, status at, or future relations with this Institution."

#### **6.35.4 Elderly and Terminally Ill Subjects**

The care, protection and considerations given to enroll elderly and terminally ill participants should be same as normal population with the exception of consideration for cognitive impairment and institutionalization. In the past, persons in nursing homes or other institutions have been selected as subjects because of their easy accessibility. It is now recognized, however, that conditions in institutional settings increase the chances for coercion and undue influence because of the lack of freedom inherent in such situations. Research in these settings should therefore be avoided, unless the involvement of the institutional population is necessary to the conduct of the research.

Points to consider:

- A. Does the proposed consent process provide mechanisms for determining the adequacy of prospective subjects' comprehension and recall?
- B. How will subjects' competence to consent be determined?
- C. Will the research take place in an institutional setting? Has the possibility of coercion and undue influence been sufficiently minimized?

Severe illness often affects a person's competence, and terminally ill patients may be vulnerable to coercion or undue influence because of a real or perceived belief that participation is necessary to receive continuing care from health professionals or because the receipt of any treatment is perceived as preferable to receiving no treatment. Two important reasons for concern regarding research involving terminally ill persons are:

- A. They tend to be more vulnerable to coercion or undue influence than healthy adult research subjects; and
- B. Research involving the terminally ill is likely to present more than minimal risk.

#### **6.35.5 Research Conducted in Patient Mental Health Facilities**

In patient mental health subjects can be subjects of any research provided that the research is conducted in strict compliance with Federal and State regulations, and facility-specific policies and procedures. Investigators interested in conducting research in a mental health facility must receive approval from the facility after explaining to the facility and patients (and their advocates) the nature of research, the expected benefit and the potential risk(s) involved in research. Researchers proposing to conduct research in such facilities should detail in their protocols how they will comply with these requirements and will include a copy of any necessary approvals from the state.



## **ARTICLE 7 - PREPARING A RESEARCH PROTOCOL**

Guidance to protocol development is provided in the website

<https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/index.html>.

Every IRB application must be accompanied by a protocol for research. The protocol must be a summary of the research plan outlined according to factors which the IRB considers essential for its review. A template for developing a protocol is available at the following link:

<https://sites.rowan.edu/officeofresearch/compliance/irb/submissions/initialsubmissions/index.html>.

### **7.1 Qualifications of the Principal Investigator (PI)**

Every research protocol will explicitly identify the PI of record. The qualifications of the PI and the investigator's professional development in relation to the degree of protocol complexity and risk to human subjects are considered in reviewing protocols. IRBs may require less experienced research investigators to be supported by seasoned researchers. Proposals that require skills beyond those held by the PI can be modified by the IRB by requiring additional qualified personnel. Only faculty and staff members may serve as PI. Students, medical research residents, fellows, and post-doctoral fellows are considered co-investigators.

For further guidance on qualification of investigators go to the following links:

<https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM328855.pdf>.

and <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/investigator-responsibilities/index.html>.

### **7.2 Who may be the Principal Investigator?**

A principal investigator is the individual who assumes full responsibility for a research project, including the supervision of any co-investigators, research assistants, house staff and students. The Institutional Review Board only recognizes one principal investigator per human subject's research study, no matter how many research sites may be involved. Other individuals may be named co-investigators. The principal investigator must possess the expertise, time and commitment to conduct and provide the necessary oversight for all aspects of the study, and must be willing to accept full responsibility for the study. In multi-site studies for which Rowan University is the coordinating institution, the principal investigator assumes the responsibility for the conduct of the study at each performance site and by each site-specific principal investigator.

The following classes of individual may serve as principal investigator on human subjects studies conducted at the Institution:

- A. Faculty that have an appointment as Professor, Assistant Professor or Associate Professor
- B. Individuals with a paid faculty appointment at the Institution, other than visiting and per-diem faculty, with the approval of the department Chair and/or

college/school Dean or Assistant/Associate Dean; unpaid (volunteer) faculty at the Institution with written justification by the Department Chair and Research Dean/Senior Associate Vice Provost for Research, and case-by-case approval by the University Institutional Official.

- B. Individuals in permanent, non-faculty staff positions at the Institution, with the approval of the department Chair or Research Dean/Vice President for Research.
- C. House staff (interns, residents and clinical fellows), postdoctoral fellows, graduate students and undergraduate students may not be principal investigators on human subject studies, but may be named co-investigator under a faculty advisor as principal investigator. The faculty advisor, as principal investigator, assumes all of the responsibilities for the conduct of the research and the work of the intern, resident, clinical fellow or postdoctoral fellow. Exceptions for individual house officers or postdoctoral fellows may be requested by the department Chair to the IRB Director if written procedures are in place to ensure appropriate close-out of the research when the individual leaves the University.

### **7.3 Determining Whether Research Involves Human Subjects**

PIs through their research design and assistance from the IRB office determine whether the proposed research is human subjects' research as defined by HHS.

Investigators must submit a Determination of Non-Human Subject Application through CIRB. All Research Protocols involving human subjects are to be submitted to the IRB Office for review. The IRB then determines whether the research is considered non-human subject research or is exempted from IRB review under applicable regulations. Determination will also be made whether full or expedited IRB review is appropriate for the proposed study.

#### **7.3.1 Categories of Research under Non-Human Subject Research**

- A. Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
- B. Public health surveillance activities, including the collection and testing of information or, biospecimens, conducted, supported requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

- C. Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
- D. Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.
- E. Information that is publicly available. Some of the databases listed below contain publicly available data sets as well some restricted use component. Publicly available data sets are not subject to the definition of human subject research as long as the following criteria are met (an IRB determination of non-human subject research subject is still required):
  - a. Research will not merge any data sets in such a way individuals may be identified and
  - b. Research will not enhance the publicly available data sets with identifiable, or potentially identifiable data.
  - c. Publicly available data set may itself contain identifiers. Use of such identifiers are permitted so long as they are not linked to additional private identifiable information in researcher's possession.

Below are the links to some of the publicly available data sets.

- i. National Trauma Data Bank (NTDB) <https://www.facs.org/quality-programs/trauma/ntdb>.
- ii. National Cancer Database (NCDB): <https://www.facs.org/quality-programs/cancer/ncdb/puf>.
  - a) Center for Disease Control (CDC): Behavioral Risk (BRFSS): <https://www.cdc.gov/brfss/>.
  - b) Youth Risk Behavioral Survey Study (YRBSS): <https://www.cdc.gov/healthyouth/data/yrbs/index.htm>.
  - c) National Ambulatory Medical Care Survey (NAMCS) National Hospital Ambulatory Medical Care Survey (NHAMCS): [https://www.cdc.gov/nchs/ahcd/about\\_ahcd.htm](https://www.cdc.gov/nchs/ahcd/about_ahcd.htm).
  - d) dbGAP: National Center for Biotechnology Information: <https://www.ncbi.nlm.nih.gov/>. NOTE: All datasets except those which specifically require IRB approval. It is the PI's responsibility to ensure that proper documentation is procured prior to use of the data.
  - e) Data Resource Center for Child & Adolescent Health: <http://childhealthdata.org/>. And <http://childhealthdata.org/learn/pathways>.
  - f) National Cancer Institute: <https://tcga-data.nci.nih.gov/docs/publications/tcga/>?
  - g) National Center for Education Statistics (NCES): <https://nces.ed.gov/>. And Public-Use Data Files including, but not limited to: School Survey on Crime and Safety (SSOCS): <https://nces.ed.gov/surveys/ssocs/>.
  - h) National Data Archive on Child Abuse and Neglect: <https://www.ndacan.cornell.edu/>.

National Survey of Child and Adolescent Well-Being (NSCAW - General Use Files Only):

<https://www.acf.hhs.gov/opre/research/project/national-survey-of-child-and-adolescent-well-being-nscaw>.

- i) National Study of the Incidence of Child Abuse and Neglect:  
<https://www.childwelfare.gov/topics/systemwide/statistics/nis/>.
- j) U.S. Department of Agriculture (USDA) - Food and Nutrition Assistance Research Database: <https://www.ers.usda.gov/data-products/food-and-nutrition-assistance-research-reports-database/>.
- k) U.S. Department of Energy (DOE) - Comprehensive Epidemiologic Data Resource: <https://apps.orau.gov/cedr/#.WkPsFE2WxhF>.
- l) U.S. Food and Drug Administration (FDA) - CFSAN Adverse Event Reporting System (CAERS):  
<https://www.fda.gov/Food/ComplianceEnforcement/ucm494015.htm>.
- m) University of Michigan Institute of Social Research  
Panel Study of Income Dynamics (public version only):  
<https://psidonline.isr.umich.edu/>.  
Health and Retirement Study (public version only):  
<http://hrsonline.isr.umich.edu/>.

Inter-University Consortium for Political and Social Research (ICPSR) (public version only): <http://www.icpsr.umich.edu/icpsrweb/ICPSR/index.jsp>.

There could be other publicly available data sets that researchers at the Institution are aware of. If such publicly available data sets are going to be used, researchers are required to provide information about such sources to the IRB Office along with an CIRB application for “Non-Humans Subject Research.”

- F. Private information or biospecimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems if following conditions are met:
  - a. The private information or biospecimens were not collected specifically for the currently proposed project through an interaction or intervention with living individuals and
  - b. The investigator(s) cannot readily ascertain the identity of individual(s) to whom the coded private information or specimens pertain because:
    - i. The investigator and the holder of the key enter into an agreement prohibiting the release of the key to investigators under any circumstances, until the individuals are deceased;
    - ii. There are IRB-approved written policies and procedures for a repository or data management center that prohibit the release of the key to investigators, until the individuals are deceased.

In all of the scenarios listed in this section investigators are required to submit an CIRB application. Investigators must submit the application choosing “Non-Humans Subject Research” category.

#### 7.4 Unaffiliated Investigator Agreements

The engagement in human research activities of each independent investigators who is not an employee or agent of the Institution may be covered under the Assurance only in accordance with a formal, written agreement of commitment to relevant human subject protection policies and IRB oversight. Clinical trials and other research involving research personnel not affiliated with the Institution must complete the Institution's Site Investigator Study Agreement.

<https://sites.rowan.edu/officeofresearch/compliance/irb/submissions/initialsubmissions/index.html>). **Go to Submission Guidance section to downloads the form.**

These agreements are for individual physicians and research collaborators operating in private settings or other institutions that are not covered under our Institution's Assurance. The Institution maintains these commitment agreements on file and provides copies to OHRP upon request.

### **7.5 Roles and Responsibilities of Principal Investigator**

For every research protocol, the PI of record shall specifically identify in writing all other investigators who will actively participate in the research and in securing informed consent from subjects.

The responsibilities are:

- A. Preparation of a research protocol and fulfillment of all subsequent obligations in connection with that protocol and strict compliance with all applicable regulations.
- B. PI will not make any changes in the design or conduct of the research including addition of new subjects without the IRB approval. Exceeding the number of subjects to be enrolled beyond what has been initially approved by the IRB requires IRB approval.
- C. PI may change the protocol without IRB approval when it is necessary to eliminate apparent immediate hazards to human subjects. When such protocol deviations are done for the safety of subjects, it must be immediately reported to the IRB.
- D. PI will make every effort to minimize risk by using procedures which are consistent with sound research by reducing unnecessary risks using appropriate procedures.
- E. PI must ensure that risks to subjects are reasonable in relation to anticipated benefit (if any).
- F. Selection of subject population is equitable.
- G. Obtain informed consent in advance of research participation.
- H. Ensures that privacy and confidentiality is properly maintained.
- I. Appropriate additional safeguards are included in the study to protect the rights and welfare of human research subjects who are likely to be vulnerable to coercion or undue influence (e.g., children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons).
- J. PI is responsible for properly implementing an approved protocol using good clinical and/or human subject research practices.

- K. PI is responsible for coordinating, supervising and monitoring the activities of all other persons participating in the research and for assuring that all personnel are properly trained to conduct human subject's research.
- L. PI is also responsible for timely submission of documents (21 days before the expiration date of an approved protocol) for the **continuing review** of the project, including reporting to the IRB all changes in the research activity, including amendments and all unanticipated problems (adverse events) involving risks to human subjects.
- M. If a protocol has expired, NO subject enrollment should occur and all research activities must be stopped. **Research activities include but are not limited to recruitment and enrollment of subjects, collection of specimens, surveys, review of medical records or other health information, and the performance of research tests/procedures, treatment or follow-up on previously enrolled subjects.**
- N. If treatment and/or follow-up of subjects are necessary for subject safety and welfare, the IRB must be informed in writing immediately. Either the Chair or IRB will consider these requests on a case-by-case basis so treatments are continued until the study is re-approved by IRB. Federal regulations require that the IRB consider only what is in the best interest of the subjects when determining whether continuation of previously enrolled subjects is appropriate while continuing review is in process.
- O. PI's are encouraged to attend the meeting to respond to questions raised by the committee's review of the proposal. The substitution of PI's by their research coordinator or student is discouraged. The PI, research coordinator and/or student will be excused for the actual review and vote.
- P. The PI is responsible for complying with all IRB decisions, conditions, and requirements and for ensuring that applicable laws and regulations are observed.
- Q. Unanticipated adverse events that are also unanticipated problems involving risks to subject or others (e.g., those that are related and or possibly related to the research) must be reported to the IRB and other appropriate agencies as they occur. Further guidance on reporting external un-anticipated adverse events and local unanticipated adverse is available at:  
<http://www.hhs.gov/ohrp/policy/advevntguid.html>. and  
<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf>.
  - a. To report to adverse events to sponsors (Clinical trials), use forms supplied by the sponsor. In January 2009, FDA issued further guidance on reporting adverse events. The purpose was to distinguish between adverse events that are unanticipated problems that must be reported to IRBs from those that are not. For further information on adverse event reporting go to <http://www.fda.gov/downloads/drugs/guidancecompliance/regulatoryinformation/guidances/ucm079753.pdf>.

## 7.6 Additional Responsibilities of a Principal Investigator

- A. Protecting the rights and welfare of the participants.
- B. Ensuring that the research receives IRB review and approval before any activity begins, including screening procedures.
- C. Ensuring that all co-investigators and research staff comply with the conditions, findings, determinations and requirements of the IRB.
- D. Ensuring that all pertinent regulations, laws, guidelines and procedures are observed by all co-investigators and research staff involved in the conduct of the study.
- E. Identifying all collaborating sites in the protocol, indicating which aspects of the research will take place at each site, and ensuring that there is appropriate IRB review and approval at each site.
- F. Assuring receipt of IRB approval from all collaborating institutions.
- G. Ensuring that all co-investigators and study staff submit disclosures of financial and other personal interests in the study to the Research Dean and the IRB.
- H. Ensuring that the protocol is followed in the conduct of the study, including inclusion/exclusion criteria, number of subjects recruited, obtaining consent, etc.
- I. Ensuring that studies receive timely IRB continuing review and approval.
- J. Obtaining prior IRB review and approval of all changes to the protocol and consent forms, except where necessary to eliminate immediate hazards to subjects or others.
- K. Reporting to the IRB promptly any unanticipated problems involving risks to subjects or others, and any serious adverse events that are either unanticipated or anticipated.
- L. Ensuring adherence to all HIPAA requirements.
- M. Ensuring that the IRB is notified about any monitoring visits or FDA audits in advance of the visit, as well as the results of any such visits.
- N. Discontinuing all study activities at the end of the IRB-designated approval period;
- O. Submitting to the IRB all required study-closure documentation upon study completion or discontinuation.

## 7.7 Required Components of a Research Protocol

Required Components of a Research Protocol.

Follow specific directions on the IRB website at

<https://sites.rowan.edu/officeofresearch/compliance/irb/index.html>. For help with CIRB submission process please click the link "CIRB" on the CIRB website at

<https://sites.rowan.edu/officeofresearch/compliance/irb/index.htm>. All new, initial, continuing review, amendments, reportable events and Final Reports must be submitted electronically via CIRB.

Every IRB application must be accompanied by a protocol for research. The protocol must be a summary of the research plan outlined according to factors which the IRB considers essential for its review. Please access the IRB protocol template at

<https://sites.rowan.edu/officeofresearch/compliance/irb/index.html>. Please paginate the page and include the protocol version number as a footer.

The research protocol prepared by the PI must describe the study with sufficient detail and clarity that all members of the IRB, including non-scientific members, are able to determine its nature, intent, and scope, as well as the types and degrees of risk to subjects and the provisions for the protecting the rights and welfare of subjects.

### **7.7.1 Purpose/Specific Aims**

Clearly state the overall purpose of the study. [Note: IRB reviewers come from a diversity of backgrounds. Therefore, avoid the use of acronyms and highly technical language.]

- A. Objectives: Create objectives—statements outlining specifically what will be achieved by the study—that derive directly from the overall purpose.
- B. Hypothesis: Express scientific hypotheses—statements about expected relationships between variables— that are testable and that include measureable outcomes/endpoints as described in the Research Design and Methods section of the protocol. Hypotheses correspond directly to the objective(s).
- C. Storage, maintenance use of identifiable private information or identifiable biospecimens for secondary research using Broad Consent.

### **7.7.2 Background and Significance**

Provide a succinct review of the relevant scientific literature to justify the proposed study. Include key references but not a complete literature review. Include relevant preclinical data, such as animal studies or other human studies utilizing similar drugs, devices, procedures, leading up to, and supporting the proposed research, if applicable. Address the importance of the knowledge that may reasonably be expected to result for your discipline (e.g., clinical, diagnostic, etc.) and to society generally (e.g. increased understanding of disease, etc.).

### **7.7.3 Research Design and Methods**

Describe the design of the study (cross sectional, descriptive, case/control, retrospective chart review). Justify how this design addresses the research objectives and hypotheses. If applicable, describe procedures for randomization of subjects' care or assignment to interventions.

### **7.7.4 Duration of Study**

Define the duration of the study and the length of time each subject will participate in the study.

### **7.7.5 Study Sites**

List the sites where research will be conducted.

### **7.7.6 Sample Size Justification**



Describe total sample size (including gender and minority considerations), expected accrual rates and sampling strategy (justified for testing the primary and/or secondary hypothesis). Power calculations for proposed sample size and endpoints should also be included. Give references for the pilot data and method of sample size calculation.

#### **7.7.7 Subject Selection and Enrollment Considerations**

Selection and enrollment design considerations are extremely important for assuring human subjects' protections, including their voluntary & informed consent, privacy of person and confidentiality of data, and equitable access to research.

#### **7.7.8 Inclusion Criteria**

Describe the target subject population. Provide all relevant demographic (e.g., age, ethnicity), biomedical (e.g., disease status, laboratory values, pregnancy) and behavioral characteristics (e.g., cognitive abilities, mood) relevant for inclusion and exclusion. [Note: In order to assure all persons equitably share the burdens and benefits of research, scientific objectives, not membership in a privileged or vulnerable group, must guide the development of inclusion criteria.]

#### **7.7.9 Exclusion Criteria**

Describe what relevant demographic, biomedical or behavioral characteristics exclude persons from participating in your research. Provide clear justification(s) for exclusions. No group of persons—women, pregnant women, children, minorities, non-English speaking persons—should be categorically excluded from the study without a scientific or ethical reason to do so. Notice and document any efforts to overcome any anticipated barriers to participation. [Note: If a study is to offer value to future patients, its results must be generalizable. This means that the sample of subjects selected for the study must be representative of society's members.]

#### **7.7.10 Subject Recruitment**

Describe how, when, and by whom individuals will be recruited to participate in the study. Explain how individuals will be approached, what collateral materials will be used to recruit them (e.g., flyers, internet, letters from physicians), and the context of the offer of participation (location, timing of offer, and decision deadline). Provide copies of all recruitment materials in an appendix to the protocol. Indicate the number of subjects to be approached for recruitment, allowing for screen failures and/or drop outs. Carefully consider how/if others (e.g., family members) become secondary subjects as a result of the information provided by the primary subjects and how such persons will be protected if that occurs.

#### **7.7.11 Consent Procedures**

Describe the consent procedures to be followed, including how, when, where and by whom informed consent will be obtained and documented. [Example: The study will be explained to the potential subject by the Principal Investigator, the consent will be read, and their questions will be answered. If he/she wishes to enroll, the subject will sign the

consent form. The study staff obtaining consent will also sign and date the consent form, and a copy will be given to the subject.] Be mindful to create an environment that supports voluntary and informed decision-making and include additional safeguards for persons likely to be vulnerable to coercion or undue influence. Procedures must reflect that informed consent will be sought from each prospective subject or the subject's legally authorized representative. A copy of the consent document(s) you will use must accompany your IRB application. Under certain circumstances, a waiver of consent may be necessary. If so, a request for a waiver must be submitted to the IRB for their consideration/approval. [Note: Informed consent is not an event but a process. Study staff should periodically check with subjects to answer any further questions they may have about the study or their rights while participating in it.]

#### **7.7.12. Subject Costs and Compensation**

List all costs, if any, that subjects will likely incur, such as, parking fees, travel expenses, food, over-the-counter or prescription drug costs. Likewise, list all expenses that will be covered by the research, such as study drugs or tests. Indicate what compensation, if any, will be provided and whether it will be pro-rated depending on what parts of the study the subject completes.

#### **7.7.13 Chart Review Selection**

Chart reviews require investigators to submit "Preparatory to Research Form" available on the following link:

[https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1\\_27](https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1_27). and approval from the Privacy Officer. Such approval must be uploaded to CIRB application.

For IRB review, describe who and how charts will be accessed for retrospective chart review. Explain the parameters you will use to select charts and where will you review these charts to abstract data. Provide a data log or excel spread sheet with the relevant variables you plan to collect. The information collected should be directly relevant to the objectives and hypotheses for the research. Explain when and how identifiers will be removed from the data collected. If a waiver of consent is granted, identifiers should be destroyed with no possibility of linking the data with these identifiers as soon as possible. This affords respect and privacy protections to persons whose data was reviewed/used without their consent.

To prepare protocols for medical chart review, researchers are directed to complete the protocol template for medical chart review available in the following link:

<https://research.rowan.edu/officeofresearch/compliance/irb/submissions/initialsubmissions/index.html#A1>.

#### **7.7.14 Study Variables**

**7.7.14 (a).** Independent Variables or Interventions: Describe any treatments or interventions to be compared for their effects on participants. Clearly differentiate

interventions or procedures that are a part of standard of care from those that are experimental. In the case of chart reviews, indicate if you will be comparing specific treatments or other interventions performed in the past. All procedures and interventions must be consistent with sound research design and should not unnecessarily expose subjects to risks of harm.

**7.7.14 (a) (i).** Drug or Device Interventions: Include the regimen (drugs, doses and schedule by which the treatment will be given), and drug administration guidelines (i.e., route of administration, infusion solution, concentration if applicable, rate of infusion and how the drug is packaged). Describe fully and clearly how all study drugs are prepared and administered, including special precautions. Provide FDA investigational new drug (IND) or investigational device (IDE) information as applicable.

**7.7.14 (b).** Dependent Variables or Outcome Measures: Describe all study instruments such as questionnaires, behavioral measures, laboratory tests, or medical evaluations (e.g., history/physical, X-rays) that are not a part of standard clinical practice and are being performed specifically for the purpose of the research. Wherever possible, describe in lay terms the amount of specimen to be taken (e.g., blood in tsp.; tumor tissue). Include copies of all tests and questionnaires. For chart reviews, clearly define the information you will be extracting from the chart with justification for the information collected.

#### **7.7.15 Risk of Harm**

Fully describe physical, psychological/emotional, social, legal and economic risks of harm that are possible to affect subjects as a result of study interventions and/or outcomes. Do not describe risks and benefits of standard therapies subjects will receive regardless of their participation in the research. Discuss these risks in the context of potential benefits of participation in the research and how reasonable these risks are in relation to benefits.

#### **7.7.16 Potential for Benefit**

State potential benefits for the individual and/or society, being careful not to overstate benefits. Almost all research studies—even those with minimal risk—has the risk of loss of subjects' privacy and confidentiality of data collected or produced. In addition, the research may involve a risk to certain communities or groups of individuals. Determine if any data collected are sensitive (e.g., alcohol, drug use, sexual) and whether a Certificate of Confidentiality will be requested. For all risks of harm listed, address how these risks will be minimized (e.g., whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes) and how they are justified.

### **7.8 Data Handling and Statistical Analysis**

Provide a data analysis plan that is logical and appropriate for endpoints selected. The plan should not introduce bias through exclusion of subjects from analysis. Describe data entry, editing and methods for quality assurance. Indicate how information will be recorded (e.g., electronically, audio, paper), where data will be stored, who will have access, and how subject's privacy and confidentiality of health information will be protected during collection, storage, use, or transmission (e.g., flash drives, internet) of data. Document when the link between personal health identifiers and data will be destroyed, if ever. Consider, particularly for chart review, destroying the link as soon as possible. Document how long the investigator will keep the data [should be a minimum of 6 years]. Describe the statistical methods to be employed. Clinical relevance of the results as well as statistical significance should be discussed. Describe and justify any interim analyses.

### **7.9 Data and Safety Monitoring**

For all studies of greater than minimal risk, a safety monitoring plan must be included to ensure the safety of subjects. This plan should include procedures for monitoring the safety of the study, procedures for the sponsor and the IRB, and plans for interim safety reviews. Adverse events need to be defined with information on how they will be managed and reported. Provide a plan for emergency care and/or clinical management of adverse events as needed (e.g., uncovering of suicide risk). Explain how you will know if the study is causing undue burdens or harms to subjects. Include the frequency and type of assessments you will use to determine safety of subjects throughout the study.

If the study is greater than minimal risk, you may consider or be required to create an independent Data and Safety Monitoring Board (DSMB) or Data Safety Monitoring Committee (DSMC). If such a board is planned or required, the IRB will need information on the composition and credentials of the monitoring group, their frequency of meetings and reporting procedures.

### **7.10 Reporting Results**

#### **7.10.1 Individual Results**

Describe your plan for notifying subjects of study or individual test results that have clinical importance (e.g., abnormal lab values on screening). If providing individual results, provide evidence of appropriate lab certifications (e.g., CLIA) and the qualification(s) of the study staff who will return such results.

#### **7.10.2 Aggregate Results**

Describe your plan for notifying subjects of aggregate research results, as applicable. (Note: Studies show that a primary reason persons enroll in research is to make a meaningful contribution to the future health of others. Returning aggregate results to subjects respects and recognizes their contributions to research.)

#### **7.10.3 Professional Reporting**

Describe your plan to share the results of your research with the scientific community.

### **7.11 Bibliography**

Include all references cited in the text.

### **7.12 Additional Considerations**

#### **7.12.1 Sponsor Protocols**

Any protocols or other information (including investigational drug or device brochure) about an investigational drug or device prepared or compiled by the sponsor of the research or any organization identified in **Article 7.7.2.N** of these Guidelines. Any amendments to a sponsor's Protocol, consent form; assent form whether made by the sponsor or by the PI, must be included or submitted to the IRB as the changes/amendments become available.

#### **7.12.2 Research Involving Investigational Drugs or Devices**

- A. The protocol must include an explicit statement that the proposed research involves an investigational drug or device.
- B. The PI must indicate whether it is an Investigational New Drug ("IND") or has an Investigational Device Exemption ("IDE") pursuant to FDA regulations at 21 C.F.R. 812.
- C. PI must provide the IND or IDE number whether the drug or device is approved for investigational use in the manner proposed in the protocol submission.
- D. If it is an internally-initiated trial involving a new drug or off-label use of an approved drug, procedures to obtain IND and IDE numbers from the go to: <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm>.
- E. When PI makes an IND application, a copy of the IND application must be given to the IRB.
- F. When IND is approved by the FDA, a copy of the FDA approval or any other communication that has been sent to or received from the FDA must be provided to the IRB.
- G. PI is required to submit IND safety reports to the FDA and IRB annually.

#### **7.12.3 Studies involving Multiple Diseases**

If a study involves multiple targeted diseases, a separate study protocol and separate study consent form must be submitted for each of the targeted diseases. An omnibus protocol for multiple studies is not permitted. Likewise, if control groups are receiving no treatment or different treatment compared to experimental group, a separate consent form is required for the control group.

#### **7.12.4 Tips on Subject Recruitment and Selection**

Defining the group of subjects to be enrolled in a research project involves a variety of factors, including:

- A. Requirements of scientific design;

- B. Susceptibility to risk;
- C. Likelihood of benefits and what they might be
- D. Practicability of recruiting subjects and
- E. Fairness - Since a primary aim of clinical research is to provide scientific evidence leading to a change in health policy or a standard of care, it is imperative to determine whether:
  - a. The intervention or therapy being studied affects women, children, or men and populations of minority groups differently;
  - b. Equitable selection of subjects and the applicability of study results generally require investigators to strive for gender balance in the study population;
  - c. Women, children, and members of minority groups must be included in all research projects involving human subjects unless a clear and compelling justification establishes to the satisfaction of the IRB that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research;
  - d. If a proposed project includes a study population in which women and minorities are not appropriately represented, the PI must provide "a clear compelling rationale for their exclusion or inadequate representation.";
  - e. Factors such as inconvenience (e.g., time required, travel involved, or restrictions on diet or other activities), discomfort, and embarrassment and burdens of participating in research must also be considered in planning study enrollment and
  - f. Detail the procedures for subject recruitment and selection as follows:
    - i. Provide the number to be recruited at this institution and elsewhere (multicenter studies), ages, and sex of prospective subjects.
    - ii. Describe any inducements or remuneration to be offered to subjects (e.g., cash payments, free hospitalization, medication, clinical testing) (See Article 3.6).
  - g. Summarize the methods of recruitment to ensure subjects from a variety of sources have chances of being selected, such as:
    - i. Notices on bulletin boards and advertisements to encourage; participation of subjects from a broad cross Article of the community or personally recruit subjects from community health clinics;
    - ii. Provide the name of the hospital and the inpatient service;
    - iii. Outpatient clinic, school, business, or other agency from which subjects will be recruited and
    - iv. Indicate any "special" or "vulnerable" categories of subjects, i.e., mentally disabled persons, minors, pregnant women, and prisoners.

#### **7.12.5 Tips on Site Selection**

- A. Identify the specific name of the hospital, inpatient service, outpatient clinic, school, business, or other agency from which subjects will be recruited.

- B. For locations other than the Institution's facilities, submit documentation to support that responsible authorities at the research location agree to facilitate the project. Such documentation must be provided before IRB approval. IRB may conduct an inspection of Off-site location.
- C. When any part of the research is to be conducted at an institution not affiliated with the Institution, the PI must submit written documentation that the relevant portions of the research have been, or will be, approved by a duly constituted IRB at that institution.
- D. Such documentation indicating the approval letter from that institution and any approved consent forms thereof including indemnification of Rowan University must be provided prior to IRB approval.
- E. In the absence of an IRB at the other institution, review will be conducted by one of the Institution's IRBs.
- F. The PI must be aware that special issues arise when a subject participating in a research study at one institution is admitted to another medical facility. The FDA provides some guidance on how research may proceed at another institution. The guidance for use of investigational products when subjects enter a second institution is available at:  
<http://www.firstclinical.com/regdocs/doc/?db=FDA Sheet Second Institution>  
All three scenarios described at this website must be reviewed and applied as needed.

#### **7.12.6 Tips on Research Design**

Prepare an orderly scientific description of the intended procedures as they directly affect the subject and include:

- A. The number and estimated length of hospitalizations, length of time for various procedures (e.g., interviews, completing questionnaires), frequencies with which procedures may be repeated, randomization, and any manipulation which may cause discomfort or inconvenience, anticipated risks, and a statement indicating that unforeseeable risks could occur during the course of the investigation.
- B. Doses, volume, and routes of administration of drugs (research and ancillary treatments).
- C. The amount, location, and frequency of blood draws;
- D. Plans for monitoring the progress of research and follow-up.
- E. Description of anticipated circumstances under which the study may be terminated or discontinued, a statement of how this will be determined and monitored, including measures to treat side effects or handle or refer problems identified during the study.
- F. A copy of any questionnaires, tests, or rating scales to be used, or, if standard instruments, the copies of those to be administered. If a questionnaire is not yet drafted, the PI should submit to the IRB a summary of types of questions or draft questions for review. The IRB may request a final copy of the questionnaire in such cases prior to its approval.

G. An application for Human Sample Registration must be submitted to IBC.

#### **7.12.7 Obtaining a “Certificate of Confidentiality” to Protect Against Compulsory Disclosure of Confidential Information**

In certain studies, protection against compelled disclosure of identifying information about research subjects may be required. In such circumstances, the NIH/HSS may authorize persons engaged in biomedical, behavioral, clinical, or other research (including research on mental health, and/or the use and effect of alcohol and/or other psychoactive drugs) to protect the privacy of subjects by withholding from all persons not connected with the conduct of the research their names or other identifying characteristic and other information derived from the research. Persons so authorized to protect the privacy of subjects may not be compelled in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals. This protection is given in the form of “Certificate of Confidentiality” issued for a particular project upon application. The guidance for Certificate of Confidentiality and the blank form is provided in the following website: <http://www.hhs.gov/ohrp/policy/certconf.pdf>. Prior IRB approval is mandatory for obtaining this certificate. . For further information and Policy go to: <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html>.

Certificate of Confidentiality (CoC) protects the privacy of research subjects by prohibiting disclosure of identifiable, sensitive research information to anyone not connected to the research except when the subject consents or in a few other specific situations. NIH funded researchers are automatically issued a CoC through their award. Other Department of Health and Human Services (HHS) agencies issue CoCs to researchers they fund. Researchers not funded by HHS can continue to apply to NIH or the FDA as appropriate to request a CoC for HHS-mission relevant research

##### **7.12.7.1 Obtaining Certification of Confidentiality for NIH and Other HHS Agencies (Non-NIH).**

Effective October 1, 2017, all ongoing or new research funded by NIH as of December 13, 2016 that is collecting and using identifiable, sensitive information is automatically issued a CoC. Awardees no longer have to apply for CoC. This policy applies to NIH funded grants, Cooperative Agreements, R & D contracts, Other Transaction Awards and NIH own intramural research. If the NIH-funded research project meets any one of the criteria listed below then such research data is automatically protected by a CoC from NIH.

Several non-NIH HHS agencies, including CDC, FDA, HRSA, and SAMHSA, issue Certificates of Confidentiality (CoCs). If your research is funded by one of these agencies or is operating under the authority of the FDA, please contact the Certificate Coordinators at the funding agency to determine how to obtain a CoC.



If your research is funded by an HHS agency other than NIH, CDC, FDA, HRSA or SAMHSA, that do not issue CoCs Health-related research you may request a Certificate of Confidentiality for specific health-related projects using sensitive, identifiable information, using the NIH online application system using the following link: <https://humansubjects.nih.gov/coc/apply>. NIH issues CoCs on behalf of these agencies.

Please direct your CoC request to the NIH Institute or Center (IC) that supports similar research. Please verify that you have the correct NIH IC with the appropriate IC coordinator at <https://humansubjects.nih.gov/coc/contacts>. before submitting an application. If you are unsure about which IC is most appropriate for your research topic, you may contact the NIH Central Coordinator at: [NIH-COC-Coordinator@mail.nih.gov](mailto:NIH-COC-Coordinator@mail.nih.gov).

#### **7.12.7.2 Obtaining Certification of Confidentiality for NIH-HHS Federal Funders.**

If your research is funded by a non-HHS Federal Agency other than HHS, you may request a Certificate of Confidentiality for a specific project that involves sensitive, identifiable information, using the NIH online application system at <https://humansubjects.nih.gov/coc/apply>.

Please direct your CoC request to the NIH Institute or Center (IC) that supports similar research. However, please verify this with the appropriate IC coordinator before submitting an application. If you are unsure about which IC is most appropriate for your research topic, you may contact the NIH Central Coordinator at [NIH-COC-Coordinator@mail.nih.gov](mailto:NIH-COC-Coordinator@mail.nih.gov). Issuance of a CoC is at the discretion of NIH. Such CoCs are issued for research projects that are collecting or using identifiable, sensitive information are issued such as:

- Meets the definition of human subjects research, including exempt research in which subjects can be identified
- Is collecting or using human biospecimens that are identifiable or that have a risk of being identifiable
- Involves the generation of individual level human genomic data
- Involves any other information that might identify a person;

On a topic that is within the HHS health-related research mission and storing the research information collected or used in the US.

#### **7.12.7.3 Obtaining Certification of Confidentiality for Non-Federal Funders**

Health-related research that is not federally funded in which identifiable, sensitive information is collected or used, may request a Certificate of Confidentiality (CoC) for specific projects using the online application system (<https://humansubjects.nih.gov/coc/apply>). Learn more about CoCs for non-Federally funded research.

CoC requests through the online system must be directed to the NIH Institute or Center (IC) that supports similar research. However, please verify this with the appropriate IC coordinator before submitting an application. If you are unsure about which IC is most appropriate for your research topic, you may contact the NIH Central Coordinator at [NIH-COC-Coordinator@mail.nih.gov](mailto:NIH-COC-Coordinator@mail.nih.gov). Please be aware that Issuance of a CoC for non-federally-funded research continues to be at the discretion of NIH.

Certificate of Confidentiality are only issued for research projects that are: collecting or using identifiable, sensitive information when the following conditions are met:

- Meets the definition of human subjects research, including exempt research in which subjects can be identified.
- Is collecting or using human biospecimens that are identifiable or that have a risk of being identifiable.
- Involves the generation of individual level human genomic data.
- Involves any other information that might identify a person.
- On a topic that is within the HHS health-related research mission and storing the research information collected or used in the US.



## ARTICLE 8 - IRB FORMS

### 8.1 Electronic Submissions through CIRB

The CIRB system is the web-based application routing and tracking system used at the Institution. . The system will increase the efficiency of the approval and administrative processes for projects and protocols involving human subjects in research. It is designed to replace the cumbersome and paper-intensive process under which applicants apply for IRB approval of study proposals. CIRB has been developed to standardize and computerize the Institutional Review Board (IRB) at the Institution.

All submissions must be submitted electronically via CIRB. For instruction to submit, go to:

<https://sites.rowan.edu/officeofresearch/compliance/irb/submissions/initialsubmissions/index.html>. . University forms such as the Financial Disclosure Form, PCP form (Jefferson (Kennedy Hopsitals), consent form templates can be found on the IRB website at:

<https://sites.rowan.edu/officeofresearch/compliance/irb/submissions/consenttemplates/index.html>. In order to successfully fill out the form(s) on this page, investigators must first save them on their computer, complete the form(s), name the document, select save and upload form(s) into the CIRB application, where appropriate. IRB will not review handwritten applications.

The IRB Office may periodically change forms to be compliant with regulations. Thus, investigators are advised to download IRB forms from the IRB website every time they send a new submission. The IRB may reject forms 30 or more days older than the current version posted on our website. Please note that submitting IRB applications using older version of forms will result in delays to receive approval from the IRB.

For CIRB help and information, go to

<https://sites.rowan.edu/officeofresearch/compliance/irb/CIRBmanualshelp/index.html>.

### 8.2 Forms

A. The following forms are available on the IRB website:

<https://sites.rowan.edu/officeofresearch/compliance/irb/submissions/index.html>.

B. Investigator Financial and other Personal Interests Disclosure form.

(<https://sites.rowan.edu/officeofresearch/compliance/irb/submissions/initialsubmissions/index.html> ). Go to the section titled: INVESTIGATOR FINANCIAL AND OTHER PERSONAL INTEREST DISCLOSURE FORM to download the form.

C. RowanSOM Performance Site forms and instructions (May not be applicable to Rowan's Glassboro campus).

D. For studies conducted at Jefferson Health (formerly Kennedy Memorial Hospitals), attach the required IPAF form for Grants and Contracts along with the signature of the Vice President Graduate Medical Education at Jefferson Health (formerly Kennedy

Memorial Hospitals). To complete the IPAF form to be uploaded into your CIRB application, go to

<https://sites.rowan.edu/officeofresearch/compliance/irb/submissions/index.html>.

E. Authorization agreement

Individual unaffiliated Investigator agreement

<https://sites.rowan.edu/officeofresearch/compliance/irb/submissions/initialsubmissions/index.html>.

F. IRB Consent form Templates are posted on the following website

<https://sites.rowan.edu/officeofresearch/compliance/irb/submissions/consenttemplates/index.html>.

These template forms include the following:

- A. Adult consent form template (latest version)
- B. Assent form
- C. Short Form – English version
- D. Surrogate consent
- E. Humanitarian Device Exemption (HDE) Consent
- F. Audio/video tape addendum to consent form template
- G. Short Form Consent in alternate languages
- H. Information sheet for participants
- I. Boilerplate consent form for use and storage of identifiable private information and identifiable biospecimens.

### 8.3 CIRB Study Applications

Investigators may access CIRB through the IRB website at

<https://sites.rowan.edu/officeofresearch/compliance/index.html>. Select “Institutional Review Board” then select “Submission” and select appropriate items listed under “submissions” for initial review, continuing review (Progress Report), modifications, protocol template and consent form templates as needed. The following applications are available on the CIRB website at <https://CIRB.rowan.edu>

- A. Initial Application
- B. Continuing Review Application includes Final Report Applications
- C. Modification Request Application
- D. Reportable Event Applications includes reportable event application, protocol deviation/violation application, DSMB Report application.
- E. There are specific guidelines for surrogate consent. Please go to <https://research.rowan.edu/officeofresearch/compliance/irb/submissions/consenttemplates/surrogateconsent/index.html> for additional information on surrogate consenting.
- F. IRB forms and CIRB applications for continuing reviews, Progress Report & final reports

[Note: If approval for continuation is not granted prior to the expiration date of the protocol, all recruitment and subject enrollment must stop. Currently enrolled subjects should continue to receive treatment and follow-up that is in

their best interest. Consistent failure to submit timely requests for continuing review is reportable to the FDA, OHRP, and the study sponsor]

- G. IRB forms and applications for study changes (Modifications) and reports
- Investigators are responsible for reporting any changes to the protocol to the IRB before the changes are instituted. These can include adding or removing study personnel, adding or revising study advertisements, updating FDA form 1572s, sponsor protocol amendments and revisions to investigator brochures, modifications to the consent and assent documents, etc.
1. Changes which are not substantive and do not affect the risk to benefit ratio for subjects may qualify for expedited review.
  2. Changes that are substantive and affect the risk to benefit ratio for subjects must be reviewed by the full board.

If there are any questions about a particular form, please contact either the RowanSOM IRB or Glassboro/CMSRU IRB.

## **ARTICLE 9 - DEPARTMENTAL REVIEW**

### **9.1 Submission to Department Chair**

The IRB requires the approval of the Chairperson of the Investigator's academic or administrative department (or the Chair's designate) indicating that the Chair has reviewed the proposal and approves of its submission to the IRB. This Departmental Approval is based on the scientific merit of the proposed research and the Chair's verification that the investigator is credentialed, has appropriate training to conduct the study, and has adequate resources and staff to perform the procedure outlined in the protocol.

If the Principal Investigator happens to be a department chair, the Senior Associate Dean for Research will review and sign off the study and the financial disclosure form on behalf of the department chair.

Department chairs are trained to perform the review on the CIRB site. Department chairs will enter the reviewer notes as required on the site. Instructions to perform departmental review are posted at:

<https://sites.rowan.edu/officeofresearch/compliance/docs/irbdocs/CIRBhelpdocs/SOMCIRBQuickReferenceGuideDepartmentReviewer-Final.pdf>.

### **9.2 Approval Process**

If the IRB study requires additional information or clarification prior to department approval, Department chairs will send questions to the study staff by selecting the "Request Changes" activity.

Department chairs will issue approval or disapproval to finalize studies by clicking on the "Issue Department Approval" or "Issue Disapproval" activities.

## ARTICLE 10: FDA-REGULATED RESEARCH

### 10.1 Special Procedures and Criteria for Approval of Research Involving Investigational Devices

If the Research Protocol involves an investigational device, two (2) separate determinations by the IRB are required.

- A. Does the Protocol involve a significant risk (SR) or a non-significant risk (NSR) to the human subjects?
- B. Is the Research Protocol approvable pursuant to the criteria established in these Guidelines?
- C. The Investigational Device Exemption (IDE) regulations describe two types <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046164.htm> of device studies, "significant risk" (SR) and "non-significant risk" (NSR).
- D. A "**significant risk**" device study involves an investigational device that:
  1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
  2. Is purported or represented to be for use in supporting or sustaining human life and presents a potential for serious risk to the health, safety or welfare of a subject;
  3. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety or welfare of the subject; or
  4. Otherwise presents a potential for serious risk to the health, safety or welfare of a subject.
- E. A "**non-significant risk**" (NSR) device study is one that does not pose a "significant risk" as defined above. Examples include most daily-wear contact lenses and lens solutions, ultrasonic dental scalers, and Foley catheters.

A nonsignificant risk device study requires **only IRB approval** prior to initiation of a clinical study. Investigators of studies involving nonsignificant risk devices are **not** required to submit an IDE application to the FDA for approval. Submissions for nonsignificant device investigations are made directly to the IRB of each participating institution. Investigators should present to the reviewing IRB an explanation why the device does not pose a significant risk. If the IRB disagrees and determines that the device poses a significant risk, the investigator must report this finding to the FDA within five working days **[\$812.150(b)(9)]**. The FDA considers an investigation of a nonsignificant risk device to have an approved IDE when the IRB concurs with the nonsignificant risk determination and approves the study.

The investigator also must comply with the abbreviated IDE requirements under **§21 CFR 812.2 (b)**:



1. Labeling - The device must be labeled in accordance with the labeling provisions of the IDE regulations (**§812.5**) and must bear the statement "CAUTION - Investigational Device. Limited by Federal (or United States) law to investigational use."
2. IRB Approval – The investigator must obtain and maintain IRB approval throughout the investigation as a nonsignificant risk device study.
3. Informed Consent – The investigator must assure that investigators obtain and document informed consent from each subject according to 21 CFR 50, Protection of Human Subjects, unless documentation is waived by an IRB in accordance with **§56.109(c)**.
4. Monitoring - All investigations must be properly monitored to protect the human subjects and assure compliance with approved protocols (**§812.46**). Guidance on monitoring investigations can be found in Guideline for the Monitoring of Clinical Investigations.
5. Records and Reports - Investigator are required to maintain specific records and make certain reports as required by the IDE regulations.
6. Investigator Records and Reports – The investigator must assure that participating investigators maintain records and make reports as required (see Responsibilities of Investigators)
7. Prohibitions –Commercialization, promotion, test marketing, misrepresentation of an investigational device, and prolongation of the study are prohibited (**§812.7**).

NSR device studies, however, should not be confused with the concept of "minimal risk", a term utilized in the IRB regulations to identify certain studies that may be approved through an "expedited review" procedure. For both SR and NSR device studies, IRB approval prior to conducting clinical trials and continuing review by the IRB are required. In addition, informed consent must be obtained for either type of study.

- F. A sponsor (Individual Investigators are also considered as sponsors) initially makes an assessment of whether a device study presents a NSR. If the investigator believes a study is NSR, the investigator should provide the IRB with the study proposal, an explanation of why the study is NSR, and other supporting information, e.g., any reports of prior investigations. The investigator should also tell the IRB if the FDA or any other IRB has determined the study to be SR or NSR, and provide any other information requested by the IRB. The IRB may agree or disagree with the sponsor's, or other IRB's, initial SR/NSR assessment.

- G. In order to determine whether a research protocol involving an investigational device poses a SR or a NSR to subjects, the IRB should consider the nature of the harm that may result from the use of the device. If a device being investigated might cause significant harm to any one of the subjects, the study should be deemed to pose an SR. Also, if the subject must undergo a procedure as part of the investigational study e.g., a surgical procedure, the IRB should consider the potential harm that could be caused by the procedure as well as the potential harm caused by the device. Those investigations where the potential harm to subjects could be life threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure, are included among those studies that are SR.
- H. If the IRB determines that the Research Protocol poses a NSR to subjects, an IDE application is **not** required. However, **IRB approval is mandatory** before the NSR device is used.
- I. If the IRB determines that the Research Protocol does pose a SR to subjects, or if the FDA has notified a sponsor under **21 CFR §812.20(a)** that FDA approval of an IDE application is required, and then the IRB shall notify the PI and, where appropriate, the sponsor, of its SR determination. No research may begin at the Institution after an SR determination by the IRB until all of the following steps have been taken:
1. The investigator must notify the FDA in writing of the IRB's SR decision, and must submit to the FDA an IDE application that complies with **21 CFR §812.20**;
  2. The FDA will notify the investigator (sponsor) in writing of the date it receives an IDE application as described in (1) above;
  3. Either the FDA approves, by order, an IDE for the investigation or Thirty (30) days have elapsed after the date on which the FDA has indicated it received the application, unless the FDA has notified the sponsor that the investigation may not begin and the IRB approves the study pursuant to the full committee review and approval criteria outlined in Article 7.9 of these Guidelines.

For further guidance on FDA device exemptions (IDE) go to the following link:  
[https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046164.htm#non\\_sig\\_risk](https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046164.htm#non_sig_risk).

## 10.2 Procedures for the Use of Humanitarian Device Exemption

The Humanitarian Device Exemption requires the following information to be submitted for IRB review:

- A. An application form "Application for Approval of HUD Use Device for Patient Care" located in the following link:  
[https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/humanitarianusedevices.html#p7EPMc1\\_13](https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/humanitarianusedevices.html#p7EPMc1_13);

- B. A letter or document from the FDA describing that the device has been approved for humanitarian use and
- C. A brochure or an information sheet describing the device and how the device is going to be used.

FDA guidelines for Humanitarian Device Exemption are posted at:

[https://sites.rowan.edu/officeofresearch/compliance/docs/irbdocs/guidancedocs/Guidance\\_Humanitarian\\_Device\\_Exemption.pdf](https://sites.rowan.edu/officeofresearch/compliance/docs/irbdocs/guidancedocs/Guidance_Humanitarian_Device_Exemption.pdf).

Investigators are advised to use the standard of care consent form used in the hospital. Informed consent must be obtained from the patient or legally authorized representative. Submission of a research consent form is NOT required. However, the IRB reserves the right to include a research consent form, if necessary. A copy of the “Patient Information Brochure” must be given to the patient or LAR.

### **10.3 Procedures and Criteria for Approval of Research Involving Investigational Drugs**

- A. Research involving investigational drugs may be conducted only if all of the following conditions are met:
  - 1. The sponsor submits to the FDA an IND for the drug;
  - 2. Investigator obtains an IND if the study is manufactured within the institution or if the study drug is used “off-label” using a different dose, route or for different indication. (See Appendix 8 for requirements and obtaining an IND from the FDA.);
  - 3. The IND is in effect pursuant to **21 CFR §312.40 (b)** and
  - 4. The IRB has reviewed and approved the Research Protocol pursuant to the criteria set forth in Article III of these Guidelines.
- B. IRB review and approval pursuant to these Guidelines is required for all investigational uses of drugs, whether:
  - 1. They are wholly investigational (e.g., a randomized trial);
  - 2. They have some elements of treatment as well as drug evaluation (e.g., long-term open safety studies or continuation studies in patients initially treated in a controlled trial); or
  - 3. They are single-patient protocols (e.g., pilot testing of a novel idea or an individual use of a plausible product in a desperately ill patient.)
- C. IRB review and approval pursuant to these Guidelines is not required if the drug is FDA approved for a specific use but is being used solely for an unapproved use in treatment and no clinical investigation is involved.
- D. Emergency variations in dosage or proposed method of administration of an unapproved drug or device shall be reviewed in accordance with Article 7.6.
- E. IRB review and approval pursuant to these Guidelines is required if the drug is investigational under an IND number and is being used on a compassionate basis in accordance with the procedures set forth in these guidelines.

### **10.4 IND Requirements**

- A. The investigation is intended to be reported to the FDA as a well-controlled study in support of a new indication for use and intended to be used to support any other significant change in the labeling for the drug.
- B. The investigation is intended to support a lawfully marketed prescription drug product requiring a significant change in the advertising of the product.
- C. The investigation involves a change in the route of administration.
- D. Dosage level, patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product.
- E. Annual or IND safety reports must be submitted and a copy of the IND safety report must be provided to the IRB.
- F. In questionable circumstances, please submit an IND to the FDA. If an IND is submitted and if the FDA does not respond within 30 days of the IND submission, the study may proceed without the IND, but NOT without submitting the IRB with the information that the FDA has not responded. IRB then may approve the study to move forward. IND requirements apply for non-medicinal basic chemicals; biologicals used in basic research, and non-lawfully marketed drugs. Please understand that even if the FDA decides that an IND is not required, the IRB may ask for pharmacology, toxicology, and manufacturing information of a substance to be used in research subjects. If nutraceuticals are the object of the study, consult FDA to determine if an IND approval from the FDA is required.
- G. IND applications are made by the investigator naming himself/herself as the sponsor on form 1572.
- H. The Institution recommends that the investigator arrange for a pre-IND consultation with the FDA  
(<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm#preIND>. ) to obtain guidance to submit the IND application.

### **10.5 Off-label Use of an Approved Drug**

Since the early 1960s, the FDA has required that drugs used in the USA be both safe and effective. The label information on the container and package insert, in the Physician's Desk Reference (PDR), and in advertisements can indicate a drug's use only in certain "approved" doses and routes of administration for a particular condition. The use of a drug for a disease not listed on the label is considered to be "non-approved", "unlabeled", or "off-label" use. Off-label use of a drug for a research purpose is inappropriate unless approved by the FDA. The approval is given in the form of an investigational new drug (IND) number for the requested "off-label" use of a prescription drug. The disease, dose, and route of administration for an "off-label" use of a drug must be specified in the IND application.

Additional information on off label use marketed drugs, biologics and devices go to:  
<http://www.fda.gov/RegulatoryInformation/Guidances/ucm126486.htm>.

### **10.6 Research Interventions in Emergencies**

### **10.6.1 Scope**

These Guidelines do not limit the authority of a physician under federal, state, or local law to provide emergency medical treatment to a patient in a non-research context. However, where proposed dosage significantly varies from the recommended or clinically accepted dosage, or the proposed method of administration is directly or indirectly forbidden in the package insert, IRB approval **MUST** be sought. IRB may also require the investigator to secure an emergency IND number from the FDA (See Article 10.4).

### **10.6.2 Written Approval and Subsequent Report**

If the proposed emergency medical treatment involves research that is not part of the IRB approved Research Protocol, the IRB chair or a senior IRB physician member may approve the treatment in writing, and will report such action to the full IRB at its next regularly scheduled meeting. Continued use of the drug or treatment will require submission within 30 days, of the initial treatment guidelines for the use of the drug or treatment. If this becomes a research project, a Research Protocol must also be submitted to define the use and the procedure for using the drug or treatment.

### **10.6.3 Emergency Use of Unapproved Medical Devices**

An unapproved medical device is one used for a purpose or condition for which regulations require an approved application for pre-market approval under **Article 515 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 360(e)]**, but for which approval has not yet been given. An unapproved device may be used in human subjects only if it is approved for clinical testing under an approved application for an **Investigational Device Exemption (IDE) under Article 520(g) of the Act [21 U.S.C. 360(j)(g)]** and **21 CFR part 812**. However, the Food and Drug Administration (FDA) recognizes that emergencies arise where an unapproved device may offer the only possible life-saving alternative, but an IDE for the device does not exist, the proposed use is not approved under an existing IDE, or the physician or institution is not approved under the IDE. Using its enforcement discretion, the FDA has not objected if a physician chooses to use an unapproved device in such an emergency, provided that the physician later provides evidence to the FDA that an emergency actually existed.

### **10.6.4 Requirements for Emergency Use of an Investigational Device**

Emergency use is the use of an investigational device in an emergency situation. It is intended to provide patients and physicians with access to devices intended to treat life-threatening or serious diseases or conditions when there is no available alternative and no time to obtain FDA approval. Emergency use may apply even if the investigational device is being studied in a clinical trial under an IDE: if a physician needs to use the device in a manner inconsistent with the approved investigational plan; or a physician who is not part of the clinical study, wishes to use the device to treat a patient with a life-threatening or serious disease or condition. Emergency use of an investigational device may occur before an IDE is approved and when a device is not being studied under an IDE.

- A. A completed "Permission for Emergency Use of Investigational Drug/Biologic/Device for Patient Care" form must be submitted for IRB Chair's approval.
- B. Each of the following conditions must exist to justify emergency use:
  - 1. The patient is in a life-threatening condition that needs immediate treatment;
  - 2. No generally acceptable alternative for treating the patient is available and
  - 3. Because of the immediate need to use the device, there is no time to use existing procedures to get FDA approval for the use.

If all of the above criteria are met, an unapproved device may be used in an emergency situation without prior approval by FDA.

- C. The FDA expects the physician to determine whether these criteria have been met, to assess the potential for benefits from the unapproved use of the device, and to have substantial reason to believe that benefits will exist. The physician may not conclude that an "emergency" exists in advance of the time when treatment may be needed based solely on the expectation that IDE approval procedures may require more time than is available. Physicians should be aware that the FDA expects them to exercise reasonable foresight with respect to potential emergencies and to make appropriate arrangements under the IDE procedures far enough in advance to avoid creating a situation in which such arrangements are impracticable.
- D. In the event that a device is used in circumstances meeting the criteria listed above, the physician should follow as many patient protection procedures as possible. Such patient protection procedures include obtaining:
  - 1. Informed consent from the patient or a legal representative;
  - 2. Clearance from the institution as specified by their policies;
  - 3. Concurrence of the IRB chairperson;
  - 4. An independent assessment from an uninvolved physician; and
  - 5. Authorization from the device manufacturer.
- E. Reporting: If there is an IDE for the device, the IDE sponsor must notify the FDA of the emergency use within 5 days through submission of an IDE Report **(§812.35(a)(2))**. If no IDE exists, the physician should submit a follow-up report on the use of the device (description of device used, details of the case, and the patient protection measures that were followed) to:

Contact information for CDRH:  
U.S. Food & Drug Administration  
Center for Devices and Radiological Health  
10903 New Hampshire Ave, Room 5429  
Silver Spring, Maryland 20993  
(301) 796-5900

[Note: an unapproved device may not be shipped in anticipation of an emergency.]  
Nights and weekends, contact the Division of Emergency and Epidemiological  
Operations (301-443-1240 or 301 796 3400)

This follow-up report should include a summary of the conditions constituting the emergency, the patient protection measures that were followed, and patient outcome information.

The physician should, under FDA regulations as well as IRB policy, follow as many subject protection procedures as possible. These include:

1. Obtaining an independent assessment by an uninvolved physician;
2. Obtaining informed consent from the patient or a legal representative;
3. Notifying institutional officials as specified by institutional policies;
4. Notifying the Institutional Review Board (IRB); and
5. Obtaining authorization from the IDE holder, if an approved IDE for the device exists.

#### **10.6.5 After-use Procedures**

- A. After an unapproved device is used in an emergency, the physician should:
  1. Report to the IRB within five (5) days **[21 CFR 56.104(c)]** and otherwise comply with provisions of the IRB regulations **[21 CFR part 56]**;
  2. Evaluate the likelihood of a similar need for the device occurring again, and if future use is likely, immediately initiate efforts to obtain IRB approval and an approved Investigational Device Exemption (IDE) for the device's subsequent use; and
  3. If an IDE for the use does exist, notify the sponsor of the emergency use, or if an IDE does not exist, notify the FDA of the emergency use (CDRH Program Operation Staff 301-594-1190) and provide the FDA with a written summary of the conditions constituting the emergency, subject protection measures, and results.
- B. Subsequent emergency use of the device may not occur unless the physician or another person obtains approval of an IDE for the device and its use. If an IDE application for subsequent use has been filed and the FDA disapproves the IDE application, the device may not be used even in circumstances constituting an emergency. Developers of devices that could be used in emergencies should anticipate the likelihood of emergency use and should obtain an approved IDE for such uses.

#### **10.6.6 Exception from Informed Consent Requirement**

- A. Even for an emergency use, the investigator is required to obtain informed consent of the subject or the subject's legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following **[21CFR 50.23(a)]**:
  1. The subject is confronted by a life-threatening situation necessitating the use of the test article.
  2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject.
  3. Time is not sufficient to obtain consent from the subject's legal 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.
- B. If, in the investigator's opinion, immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinical investigator should make the determination and, within five (5) working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. The investigator must notify the IRB within five (5) working days after the use of the test article **[21 CFR 50.23(c)]**.

### **10.7 Emergency Use of an Investigational Drug or Biologic**

The emergency use of an unapproved investigational drug or biologic requires an IND. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND.

The need for an investigational drug or biologic may arise in an emergency situation that does not allow time for submission of an IND. In such a case, FDA may authorize shipment of the test article in advance of the IND submission. Requests for such authorization may be made by telephone or other rapid communication means **[21 CFR 312.310(d)]**.

The emergency use of test articles frequently prompts questions from IRBs and investigators. This information addresses three areas of concern: Emergency Investigational New Drug (IND) Requirements, IRB Procedures, and Informed Consent Requirements.

#### **10.7.1 Obtaining an Emergency IND**

- A. A completed "Permission for Emergency Use of Investigational Drug/Biologic/Device for Patient Care" form must be submitted for IRB Chair's approval
- B. The emergency use of an unapproved investigational drug or biologic requires an IND. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company's IND.
- C. The need for an investigational drug or biologic may arise in an emergency situation that does not allow time for submission of an IND. In such a case, FDA may authorize shipment of the test article in advance of the IND submission. Requests for such authorization may be made by telephone or other means of rapid communication **[21 CFR 312.36]**.



D. FDA contacts for obtaining an emergency IND (Use CDER for drugs, CBER for biologics, and CDRH for devices):

CBER Ombudsman: Sheryl Lard-Whiteford, Ph.D.  
CBER Assistant Ombudsman: Howard S. Balick, J.D.  
Food and Drug Administration  
Center for Biologics Evaluation and Research  
10903 New Hampshire Ave, WO71-7240  
Silver Spring, MD 20993-002  
240-402-7912

General E-mail: [cberombudsman@fda.hhs.gov](mailto:cberombudsman@fda.hhs.gov)  
[cberombudsman@fda.hhs.gov](mailto:cberombudsman@fda.hhs.gov)  
<https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm122881.htm>.

CDRH-Ombudsman  
Center for Devices and Radiological Health  
Food and Drug Administration  
W032 Room 4282  
10903 New Hampshire Avenue  
Silver Spring, MD 20993  
<https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHombudsman/default.htm>.

### 10.8 Emergency Exemption from Prospective IRB Approval

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 [21 CFR 56.102(d)]. The emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an *exemption* from prior review and approval by the IRB. The exemption, which may not be used unless all of the conditions described in 21 CFR 56.102(d) exist, allows for one emergency use of a test article without prospective IRB review. FDA regulations require that any subsequent use of the investigational product at the same institution have prospective IRB review and approval. The FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue. **Life-threatening**, for the purposes of **Article 56.102(d)**, includes the scope of both life-threatening and severely debilitating, as defined below.

- A. **Life-threatening** means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to result in immediate death. Rather, the subjects

must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

- B. **Severely debilitating** means diseases or conditions that cause major and irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, and hand, or foot, loss of hearing, paralysis or stroke.
- C. **Institutional procedures** require that the IRB be notified by completing the "Permission for Emergency Use of Investigational Drug/Biologic/Device for Patient Care" form prior to such use. Notification should be used by the IRB to initiate tracking to ensure that the investigator files a report within the five (5) day time-frame required by **21 CFR 56.104(c)**. The FDA regulations do not provide for expedited IRB approval in emergency situations. Therefore, "interim," "compassionate," "temporary" or other terms for an expedited approval process are not authorized. An IRB must convene and give "full board" approval of the emergency use or, if the conditions of **21 CFR 56.102(d)** are met and it is not possible to convene a quorum within the time available, the use may proceed without IRB approval.

**Some manufacturers** will agree to allow the use of the test article, but their policy requires "an IRB approval letter" before the test article will be shipped. If it is not possible to convene a quorum of the IRB within the time available, some IRBs have sent to the sponsor a written statement that the IRB is aware of the proposed use and considers the use to meet the requirements of **21 CFR 56.104(c)**. Although, this is not an "IRB approval," the acknowledgement letter has been acceptable to manufacturers and has allowed the shipment to proceed.

### 10.9 Exception from Informed Consent Requirement

- A. Even for an emergency use, the investigator is required to obtain the informed consent of the subject or the subject's legally authorized representative. If obtaining subject's consent is not feasible, both the investigator and a physician who is not otherwise participating in the clinical investigation must certify in writing all of the following [**21 CFR 50.23(a)**]:
  1. The subject is confronted by a life-threatening situation necessitating the use of the test article;
  2. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject;
  3. Time is not sufficient to obtain consent from a legal representative of the subject and
  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.
- B. If, in the investigator's opinion, immediate use of the test article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinical investigator should make the determination and, within five (5) working days

after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. The investigator must notify the IRB within five (5) working days after the use of the test article [21 CFR 50.23(c)].

#### **10.10 Exception from Informed Consent for Planned Emergency Research**

The conduct of planned research in life-threatening emergent situations where obtaining prospective informed consent has been waived is provided by **21 CFR 50.24**. The research plan must be approved in advance by FDA and the IRB, and publicly disclosed to the community in which the research will be conducted. Such studies are usually not eligible for the emergency approvals described above. The information sheet "Exception from Informed Consent for Studies Conducted in Emergency Settings: Regulatory Language and Excerpts from Preamble," is a compilation of the wording of **21 CFR 50.24** and pertinent portions of the preamble from the October 2, 1996 Federal Register.

#### **10.11 Life Threatening Exception to Review**

If approval is impossible due to the nature of the medical emergency, and the circumstances involve a life-threatening situation in which no standard acceptable treatment is available, the physician may proceed with emergency treatment, including use of an investigational drug or device, provided that IRB is notified within five (5) working days. **Any subsequent use of such drug or device (i.e., use on a different patient) is subject to prior IRB approval pursuant to these Guidelines.** However, it is inappropriate to deny emergency medical treatment to a second patient if the only obstacle is that the IRB has not had sufficient time to review the treatment.

#### **10.12 Emergency Subjects**

Whenever emergency care is initiated without prior IRB review and approval, the patient is not considered to be a research subject (unless for the reasons stated above in Article 7.4.5). Such emergency care may not be claimed as research, nor may the outcome of such care be included in any report of a research activity. Simply stated, DHHS regulations for the protection of human subjects do not permit research activities to be started, even in emergency, without prior IRB review and approval.

#### **10.13 Sponsor's Brochure**

For clinical trials of investigational medications or devices, the complete protocol is often provided by the sponsor and is complemented by a sponsor's brochure describing the test article in detail and reviewing the complete record of prior studies of the test article. The sponsor's brochure should list and evaluate in light of previous studies all known risks associated with use of the test medication or device. (See Article 3.5)

## ARTICLE 11. OTHER STUDIES REQUIRING IRB REVIEW

### 11.1 Medical Records and Chart Review

- A. Informed consent is needed for **prospective** examination of charts.
- B. If hospital records are going to be used for research (Example, Jefferson Hospitals's records), hospital's approval for use of hospital records/charts is required before the IRB can give approval. IRB also requires the investigator to secure approval from the Privacy Officer for examining the chart. This permission is obtained by submitting Preparatory to Research from to the Privacy Officer for approval.  
([https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1\\_27](https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1_27).)
- C. Due to HIPAA regulations, if patients' protected health information (PHI) is going to be used with patient identifiers, a consent and authorization is required from the patient for such use. Chart/record reviews without patients' identifiers may be subject to HIPAA waiver of authorization. An CIRB application for research with waiver of HIPAA authorization must be submitted. Research can only begin once IRB/Privacy Board provides waiver of authorization.
- D. Studies that involve only chart and record review sometimes pose significant risk to patients. The most common is a breach of confidentiality with exposure of private or possibly social, psychological discomfort or embarrassing information without the knowledge or consent of the patient. Such studies may also lead to recruitment of patients into future non-therapeutic studies, in a manner that may result in the patient asking how the patient's record was revealed to someone not part of the patient's therapeutic team. Even if identifiable information will not be disclosed to anyone other than the investigators, an expedited review is required for studies in this category. In some circumstances where de-identified PHI is used in a prospective manner and link to the source document or chart is maintained, a waiver of consent and waiver of HIPAA authorization request must be completed on the CIRB suite.
- E. **Existing** research information downloaded without the identifiers from databases (Electronic Medical Records) with a statement that the downloaded information does not contain any identifiers are eligible for Exempt review under Exempt Category 4. HIPAA waiver of Authorization is not required; however, IRB requires the investigator to secure approval from the Privacy Officer for examining the chart using a form for Preparatory to Research  
([https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1\\_27](https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1_27)). Preparatory to research review may be required. This permission is obtained by submitting Preparatory to Research form to the Privacy Officer for approval.
- F. **Existing** research information downloaded from individual databases for the purpose of research should attest that the data is devoid of identifiers. Use of an honest broker (Person providing data) to download and provide an attestation

that the data downloaded is devoid of identifiers is essential to secure exempt approval under Exempt Category 4.

- G. Transferring **existing** data from medical charts without identifiers (protected health information) require attestation from the investigator assuring that the data recorded in the secondary data collection instrument (research note book or Excel Spread Sheets) do not contain identifiers. In such cases, the protocol will be approved under Exempt Category 4. When exempt approval is provided by IRB, researchers are not permitted to keep a link to the chart and researchers are not allowed to revisit medical charts. However, IRB requires the investigator to secure approval from the Privacy Officer for examining the chart using a form for Preparatory to Research. Preparatory to research review may be required. This permission is obtained by submitting Preparatory to Research form to the Privacy Officer for approval.  
([https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1\\_27](https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1_27) ).  
<https://research.rowan.edu/officeofresearch/compliance/irb/submissions/initialsubmissions/index.html#A1>.
- H. Effective September 3, 2020, medical chart review requires submitting “Medical Chart Review Protocol template available on the following link;

### **11.2 Human Tissue for Research**

The use and storage of tissue primarily as a part of a clinical study requires consent and authorization from prospective subjects. The use and storage of biospecimens for secondary research (purpose to store and use of biospecimens) requires a broad consent from participants. A broad consent template is posted in the following link:  
<https://sites.rowan.edu/officeofresearch/compliance/irb/submissions/consenttemplates/index.html>.

Procurement and analysis of human specimens require human tissue registration and review by the IBC. Annual General Laboratory Training and Occupational and Blood Borne Pathogen training is required to work with human specimens. If unfixed human samples are going to be processed in the laboratory, annual laboratory safety training is required.

Collection and analysis of human specimens in a CAP laboratory is exempt from registration. Likewise, formalin-fixed pathological samples are exempt from registration.

If human specimens are used for recombinant DNA procedures, a separate recombinant DNA registration and review by IBC is required. Human specimens posing a risk above levels 3 and 4 require IBC full review.

### **11.3 Data and Specimen Repositories**

A “repository” also known as banks, bio-specimen banks, data registries or data storage is any data or human tissue, or private identifiable information derived from human data or

human tissue, which has been collected and saved for future research. Federal regulations use the global term of “repositories” when describing both data and specimens. Sometimes these repositories store identifiable private information or identifiable biospecimen or both for secondary research purposes. Therefore, a broad consent form must be used to collect, store and use such identifiable private information or identifiable biospecimen.

Repositories can be formal or informal, large or small, not for profit or commercial in nature. The data can be identified or de-identified and may or may not contain genetic information. Specimen repositories can include blood or tissue samples (such as fat cells or skin cells, saliva, urine, breast milk, semen, isolates, DNA, cell lines, and other materials derived from humans). Database is collection of information elements (i.e., data) arranged for ease and speed of search and retrieval. Most databases are now maintained electronically, but the term can also be applied to paper record systems (such as set of observations, electronic medical records, etc.). Registries are collection of information stored in a database. Registry information may come from multiple sources over a period of time, they may be coded with links to donor’s identity and controlled access to the information stored in the database. Data Repositories provide opportunities for researchers to use the material or data with or without identifiers without direct interaction with the subject. Databases and repositories are often created and maintained for purposes that are totally unrelated to research. Such purposes may include diagnosis, treatment, billing, marketing, quality control, and public health surveillance, to name just a few of the many possibilities. However, when such data is used for research purposes, it will require IRB oversight.

Non-Research Repositories & Databases: If specimens or data were originally collected for non-research purposes using a broad consent and were submitted to the repository/database without any links to identifiable private data or information, it is a repository for secondary research. Studies using specimens/data from such repositories may require broad consent from donors if donors have expressed in the broad consent that they need to know how and what purpose the specimen is going to be used.

Research Repositories & Databases: If specimens or data were collected for research purposes it is a research repository. Collection of specimens/data, repository storage or data management and use of specimens or disclosure of data are all considered “research activities”. Please also see the OHRP guidance document, “Issues to Consider in the Research Use of Stored Data or Tissues” (<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/issues-to-consider-in-use-of-stored-data-or-tissues/index.html>.)

### **11.3.1 IRB Oversight**

IRB review is required when private information or identifiable information is linked to human specimens and human data from non-research databases and repositories unless the research falls under exempt categories 7 and 8 and a broad consent has been obtained from donors. Examples that fall under IRB oversight include:

- Specimens that were collected for non-research purposes that requires identifiable information
- Use of identifiable information from a database for the purpose of recruiting human subjects for a research study

In order to receive approval of such use of identifiable information from repositories, users must submit an IRB application. Upon IRB approval, users may obtain human specimens or information about human subjects from the repositories.

Investigators intend to use human specimens or information from databases without the identifiers must make an IRB application under Exempt category 4.

### **11.3.2 Consent for obtaining Private identifiable Information or Identifiable biospecimens**

Donors who donate their specimens or information to be stored in a database repository provide a broad consent for use of their specimens for research purposes. Thus, IRB requires that investigators obtain broad consent from such donors. However, in many circumstances, obtaining informed consent from those individuals may not be feasible or practical. In those cases, the IRB may waive informed consent and documentation of consent if the following criteria are met as stipulated **45 CFR 46.116(b)**:

- a. The research involves no more than minimal risk to the subjects;
- b. The research could not practicably be carried out without the waiver of consent;
- c. The waiver (or alteration) will not adversely affect subjects' rights and welfare and
- d. Where appropriate, the subjects will be provided with additional pertinent information after participation. (This last criterion rarely applies to research involving information or specimens from databases or repositories.)

Investigators who believe that criteria listed above apply to their research, they may include a request for waiver of informed consent with their IRB application.

Investigators may also request for documentation of consent. IRB will make a determination on a case by case basis whether documentation of consent could be waived.

There may be repositories that are created and maintained specifically for research purposes with subject's research consent and or authorization. Such purposes may include databases to identify prospective subjects, patient outcome information to evaluate treatment effectiveness, and tissues samples for future research. Investigators may request for specimens or data containing identifiers, which requires IRB approval. If investigators intend to use human specimens or information from databases without the identifiable information, they must make an IRB application under Exempt category 4 or expedited review category or whichever is appropriate.

### **11.3.3 Privacy Rule**

This rule applies to all specimens, databases and registries hosted at the Institution when request are made for research purposes. As in the case of consent, donors generally

donate their specimens or information to be stored in a database/repository by providing authorization for use of their specimens and information for research purposes.

According to HIPAA privacy rule protected identifiable health information (PHI) held in repositories may not be used or disclosed for research unless:

- A. Written authorization for use and disclosure of PHI has been obtained from the subject and
- B. IRB (Privacy Board) approves and documents a waiver of the authorization requirement.
- C. The holder of the PHI receives and documents the HIPAA required representations from the investigator and determines that the research involves only one or more of the following:
  - a. Decedents' information;
  - b. De-identified information;
  - c. Limited data sets or data use agreement and
  - d. Review preparatory to research.

In certain circumstances, the IRB (Privacy Board) may approve the use of specimens or information without authorization through a waiver if the following conditions as stipulated in HHS regulations at **45 CFR 164.512(i)(2)(ii)** that:

- a. The use or disclosure of PHI involves no more than minimal risk to the privacy of individuals based on at least the following:
  - i An adequate plan to protect the identifiers from improper use and disclosure;
  - ii An adequate plan to destroy the identifiers at the earliest possible opportunity unless there is a research or a health justification for retaining them (or retention is required by law); and
  - iii Adequate written assurances that the PHI will not be reused or disclosed to another person or entity (except as required by law, for authorized oversight of the research, etc.).
- b. The research could not practicably be conducted without the alteration or waiver and
- c. The research could not practicably be conducted without access to and use of the PHI.

Investigators who believe that criteria (i), (ii), and (iii) above apply to their research should submit a request for waiver of authorization on the IRB application. If investigators intend to use human specimens or information from databases without the identifiable information, they must make an IRB application at appropriate levels of IRB review application.

Alternatives to HIPAA waiver include submitting representation requests to obtain information about deceased individuals. This does NOT require an IRB application. Investigators who believe that their research involves only limited data sets/data use agreements or reviews preparatory to research may propose use of these mechanisms. Such requests are first reviewed by HIPAA Privacy Officer and may require IRB/Privacy Board approval.



#### **11.3.4 Constructing and Managing Repositories**

IRB approval is required for developing and managing research repositories. IRB approval is not required for repositories that are not primarily constructed for non-research purposes.

Researchers who wish to develop or maintain a repository (including data/tissue banks and registries) must submit an application for IRB review and receive IRB approval before initiating any repository-related activity. IRB may approve collecting, storing and sharing the information or biological specimen stored for research purposes. The IRB will require the repository manager to incorporate and implement several protection mechanisms to store and disseminate stored information or specimens. These must include:

- Defining the purpose;
- Types of research supported by the repository;
- Defining operational parameters including personnel responsible for establishing and maintaining a repository;
- Procedures for converting non-research data base, existing research database or repository into a research repository;
- Specific conditions in which the data/specimens can be accepted along with donor's signed consent or authorization;
- Description of procedures and requirements to collect, store and disseminate stored information or specimens to ensure confidentiality and protection of subject's data or specimens;
- Where human genetic research is anticipated, information about the consequences of DNA typing (e.g., regarding possible paternity determinations) and related confidentiality risks and
- Specific actions to be taken when there is a breach of privacy or confidentiality.

Once those security and protection mechanisms are approved by the IRB, the repository may disseminate information or specimens to the investigator. However, the investigator must obtain an IRB approval to obtain information or specimens. The level of review may vary from Exempt Category 4 to Expedited review depending upon whether the information/specimen requested has identifiers or not.

#### **11.3.5 Outside Repositories**

Institution's IRB must review and approve receipt of information or specimens. The use of information or specimens must adhere to the conditions imposed by the sending institution's IRB or the repository including confidentiality and protection of health information. If investigators are requesting de-identified information or specimens, they must sign an agreement indicating that will not be requesting for information that links back to the subjects or protected health information. In such cases, investigators must submit an IRB application for non-human subject research and IRB will determine if the proposed research is non-human subject research.

If a research study is not using subjects, but is using human specimens (cell lines, biopsy specimens, etc.), describe how the specimens will be obtained. Describe whether the specimen(s) already exist or will they be collected prospectively? Describe the object of the study and research procedures. Exempt status means that subject identifiers will not be used and specimens are existing on the day the research project is submitted.

#### **11.3.6 Tissue Procurement**

- A. No tissue should be collected from Hospital Operating Room at Rowan affiliated hospitals or clinics. The Department of Pathology will obtain the tissue for your research through its Tissue Procurement Center. Obtaining tissues from subjects requires prior IRB approval and a letter of authorization from the Department of Pathology Tissue Procurement Center.
- B. A research consent must be obtained if it is a research study. A broad consent must be obtained if it is for secondary research for the storage and use of biospecimens. A waiver of consent, a waiver for documentation of consent, an authorization or a waiver of authorization is required when applicable.
- C. If tissue already exists, such as a paraffin block, it will require exempt certification from the IRB. Once the IRB approval or exempt certification has been received, IRB Investigators may contact the Department of Pathology Tissue Procurement Center to receive appropriate tissues.

#### **11.4 Research on human tissue that DOES NOT require IRB review (require IBC registration)**

- A. For research projects using established cell lines or commercial blood from commercial sources, researchers must submit an IBC application for an administrative review as part of human specimen registration for use of such material. Investigators are required to complete a form entitled “Application to Obtain Cell Lines and Commercial Blood” describing the source of human cells, cell lines or commercial blood to be used and a clear statement on why such cells are important for their study and what will be done with those cells and how they will be discarded. An IRB review is not required for laboratory research on human cells obtained from tissue repositories/banks listed below:
  - ATCC American Type Culture Collection: <https://www.atcc.org/Products/Cells%20and%20Microorganisms.aspx>.
  - NDRI National Disease Research Interchange: <http://www.ndri.org/>.
  - Coryell Repository <https://coriell.org/>.
  - Cambrex <https://www.cambrex.com/>
- B. Research on tissue obtained from certain Research Tissue Banks: Investigators are required to submit a completed “Application to Obtain Cell Lines and Commercial Blood” to the IRB before securing tissues from those sources. IRB review is not required for research on (1) non-identifiable tissue or (2) coded tissue that is provided without linked identifiable information, when the tissue is obtained outside Tissue Banks. In these cases, IRB expects that the tissue bank

which provides the tissue has specific policies and procedures for distribution of non-identifiable tissue or coded tissue without linked identifiable information to investigators. A letter from the source stating that they have procedures and policies in place must be attached to the form submitted to the IRB office.

- C. Analyses on tissue obtained from outside tissue banks:  
Appropriately qualified and certified laboratory staff must perform analyses of tissue samples maintaining privacy and confidentiality. General Laboratory Safety Training and OSHA Bloodborne Pathogen is required to work with such specimens (<https://sites.rowan.edu/officeofresearch/compliance/ibc/ibcpostlogin/training/index.html#IBCTraining>.)

### **11.5 Research on human tissue that DOES require IRB review**

#### **11.5.1. Research on samples obtained prospectively, explicitly, and solely for research**

IRB approval is required for the collection and research use of human tissue samples obtained from individuals explicitly for research purposes, for example, blood samples drawn or extra blood taken at the time of a clinical blood draw specifically for a research project, or additional tissue biopsies performed solely for research purposes during a clinically indicated endoscopic procedure. The IRB will require written consent/authorization of each research participant.

#### **11.5.2. Research on excess clinical samples obtained from tissue procurement center**

IRB review is required for any proposed research use of excess clinical samples obtained from clinical department/services, for example, the clinical laboratories (including pathology) or clinical care areas, such as the operating suites. A broad consent must be used to obtain excess tissue if the tissue is obtained, stored or used for secondary research purposes. For clinical research, IRB must approve such research and investigators obtain consent and authorization to obtain such specimens for research. The IRB will determine:

- A. *Human subjects research*, as defined by federal research regulations;
- B. Human subjects research exempt from the requirements in 45 CFR 46;
- C. Research that presents no more than minimal risk to human subjects and involves procedures in one or more of the categories of research that may be reviewed by an IRB through an expedited review procedure; or
- D. Research that requires review by the IRB at a convened meeting (full board review). These determinations are based upon the nature of the research, the source of the tissue, use and/or disclosure of identifiable health information, privacy and confidentiality protections, and whether informed consent/authorization of subjects should be required, among other factors. For review of proposals involving use of excess human materials, investigators must complete and submit the appropriate exempt (Category 4) or expedited review forms through CIRB.

### **11.6 Research on autopsy specimens and donated cadavers**

Department of Public Health Regulations require that the next of kin providing consent for an autopsy give separate consent for the use of autopsy specimens for research. Autopsy consent forms may have the language that specifically addresses research. For the use of autopsy specimens, IRB review is required. KMH's or other hospital providing the autopsy material will be responsible for review of requests for autopsy specimens to determine whether the request is permitted by the consent provided by next-of-kin.

There are also willed body programs under which generous individuals donate their bodies for scientific research. Investigators may contact the Pathology Department for further information. The IRB will review such requests for research use of cadaveric materials and provide investigators with written approval for their research files. Usually these projects are found to be research, but not human subjects research, because the materials are not derived from living individuals and the materials cannot be linked to the donor.

A broad consent is required to collect, store and use such tissue for secondary research purposes.

### **11.7 Tissue or specimens obtained from collaborators**

IRB review is required for any research limited to laboratory investigation on human materials provided to investigators by collaborators outside. The investigator must contact the Office of Research Compliance before obtaining or sending materials to collaborators. A Material Transfer Agreement (MTA) may be required to receive and send research material.

The IRB Director or IRB Chairperson will determine whether the proposed research is:

- *Human subjects research*, as defined by federal research regulations;
- Human subjects research exempt from the requirements in 45 CFR 46;
- Research that presents no more than minimal risk to human subjects and involves procedures in one or more of the categories of research that may be reviewed by an IRB through an expedited review procedure; or
- Research that requires review by the IRB at a convened meeting (full board review).

These determinations are based upon the nature of the research, the source of the tissue, use and/or disclosure of identifiable health information, privacy and confidentiality protections, and whether informed consent/authorization of subjects should be required, among other factors.

### **11.8 Secondary use of previously collected research samples**

IRB review is required for any proposed secondary use of existing samples collected previously for research. A broad consent is required for the use of biospecimens if the use is for secondary research if identifiers are required for such research. The Human

Subject Protection Administrator or IRB Chairperson will determine whether the proposed research is:

- *Human subjects research*, as defined by federal research regulations;
- Human subjects research exempt from the requirements in 45 CFR 46;
- Research that presents no more than minimal risk to human subjects and involves procedures in one or more of the categories of research that may be reviewed by an IRB through an expedited review procedure; or
- Research that requires review by the IRB at a convened meeting (full board review).

These determinations are based upon the nature of the research, the source of the tissue, use and/or disclosure of identifiable health information, privacy and confidentiality protections, and whether informed consent/authorization of subjects should be required, among other factors. The IRB will take into consideration the scope/intent of the original research project, as well as a copy of the consent form subjects signed when the sample was originally provided for the initial research use.

### **11.9 Special Samples**

#### **A. Human embryonic stem cells (hESC)**

IRB approval is required for research on existing hESC lines and for the derivation of new hESC lines. In addition, there are other special ethical, legal, financial, and institutional issues related to the research use of hESC. Investigators are asked to contact the ORRC for further information. A broad consent is required for collection, use and storage for secondary research purposes. If collection is for a primary research, IRB review is required for such use. Investigators must use consent and authorization from prospective subjects.

#### **B. Fetal Tissues**

IRB review is required for research on fetal tissue. The sole exception is the research use of cell lines derived from fetal tissue that were obtained from one of the commercial repositories/banks listed above. Other possible sources of fetal tissue include tissues from Pathology Department, outside providers of pregnancy termination services, and non-profit repositories. For use of fetal tissue, please refer to Article 6, Section on Subpart B. A broad consent is required for collection, use and storage for secondary research purposes. If collection is for a primary research, IRB review is required for such use. Investigators must use consent and authorization from prospective subjects.

#### **C. Cord blood**

For the purpose of this policy, cord blood or materials derived from a placenta are not considered fetal tissue. There are state and federal laws that govern research use of fetal tissue. Federal law prohibits the sale of fetal tissue for profit. Generally, the IRB will not approve the retention of any code or link to the identity of the woman from whom the fetal tissue originated. A broad consent is required for collection, use and storage for secondary research purposes. If collection is for a primary research, IRB review is required for such use. Investigators must use consent and authorization from prospective subjects.

### **11.10 Labeling Human Samples**

Tissue retained in research laboratories should be labeled with an alphanumeric code rather than the subject's name, initials, medical record number, date of birth, or Social Security numbers in order to protect the subject's privacy and confidentiality. When the IRB approves the retention of a link, such as a code key that could be used to identify the subject from whom the tissue was derived, the link/code key should be kept in another secure location. Specific measures taken to protect the privacy and confidentiality of the tissue/data must be described in the submission to the IRB and, whenever relevant, addressed in the research consent/authorization document. Generally, tissue samples/data sent from outside collaborators or tissue banks should not be labeled with names, birth dates, or medical record or social security numbers.

### **11.11 Transfer of samples to research collaborators outside of the Institution**

IRB must review any plan to transfer tissue to outside collaborators (academic or commercial) for research. **Exception:** The transfer of **non-identifiable** tissue from an IRB-approved tissue procurement center to another investigator may NOT require separate IRB review and approval because the IRB may have already reviewed and approved the operating policies and procedures of the tissue procurement center, which describes such transfers.

Investigators are asked to address in submissions to the IRB whether or not there are plans to transfer tissue outside of Rowan University. Whenever plans to transfer tissue to outside collaborators or tissue banks arise, after initial IRB approval, an amendment to the protocol should be submitted to the IRB for approval. The investigator must follow all other requirements in the policies for Technology Commercialization which requires a Materials Transfer Agreement.

### **11.12 Requirements for a tissue repository within the Institution**

Investigators on their protocol must describe the conditions under which data and specimens may be accepted, stored, shared and managed ensuring adequate provisions to protect the privacy of subjects and maintain the confidentiality of data. Clarify who will be using these samples and whether the samples will be distributing these samples to investigators outside the institution. If investigators are planning to give samples to outside investigators, it is acceptable, but the informed consent document must specify that samples may be given to other researchers without personal identification. Operation of the Repository and its data management center should be subject to oversight by the Institutional Review Board (IRB).

### **11.13 Protocols Lacking Definite Plans for Human Involvement (45 CFR. 46.118)**

Certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the

application or proposal. These include activities such as institutional type grants when selection of specific projects is the institution's responsibility; research training grants in which the activities involving subjects remain to be selected; and projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. These applications need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived under § **46.101 (b) or (i)**, no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in this policy, and certification submitted, by the institution, to the department or agency.

Examples of such proposed activities are:

- A. Training programs in which individual training projects remain to be selected or designed;
- B. Research, pilot, or developmental studies in which the involvement of human subjects depends on such things as the results of preliminary assessments or prior animal studies;
- C. Institutional support programs where the selection of the project is the responsibility of the institution or program administrator and when supporting agencies require review and certification for such programs, protocols are to be submitted to the IRB with as much information as is available.
- E. The protocols must include assurances that additional information will be submitted when developed and, in the case of training grants, that all trainees will submit individual protocols if human subjects are to be involved in research.
- F. The IRB may give "Expedited Review and Approval" (see Article 7.4) to such programs with the understanding that specific research protocols will be submitted to the IRB once they have been developed.

#### **11.14 Waiver for Government Research**

The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of the informed consent required in **Article 5** of these Guidelines, or may waive the requirement to obtain informed consent, if the PI demonstrates, and the IRB determines and documents, that 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. Programs under the Social Security Act, or other 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; and the research could not practically be carried out without the waiver or alteration.

#### **11.15 Pedagogical and Methodological Research**

The Institution recognizes that its colleges and schools conduct cutting-edge pedagogical programs to maximize student engagement and to provide optimal learning environment

for students in various disciplines. The IRB Office does not consider some classroom-based methodological and pedagogical activities to fall under the Common Rule definition of research i.e., systematic investigation leading generalizable knowledge. Classroom-based activities that mimic research are not designed to develop generalizable knowledge.

The Institution has always considered research involving human subjects including review of records, charts and databases, analysis of tissue samples, interviews and surveys conducted to gather information from human subjects is vital to our research enterprise. Therefore, the Institution has embraced protecting the rights and welfare of human subjects and their personal information by providing assurance to the OHRP (Office for Human Research Protection) to comply with federal regulations. When students have priori intention to collect data that are part of investigator-initiated research that may include undergraduate or graduate students, part of their thesis or dissertation leading to systematic investigation and contributing to generalizable knowledge, they must submit an CIRB application for IRB review and secure approval to cover their conduct of research activities. No research activity should commence unless and until the research project has been approved by the IRB.

#### **11.16 Thesis or Dissertation Narratives**

If a research study is part of Master's or Ph.D., thesis, or an internally initiated clinical or non-clinical study, a narrative such as the research proposal submitted to the thesis committee should be provided to the IRB along with an IRB application (at an appropriate level of review) to evaluate risks associated with such studies.

#### **11.17 Guidelines for Student Conducted Research**

Faculty Advisors are responsible for all students, medical students, residents, fellows research projects. No student(s), residents or fellows can be a principal investigator.

Any research conducted by students (graduate or undergraduate), that falls under the definition of a research, using human beings as subjects and that contributes to generalizable knowledge, must be reviewed and approved by the IRB prior to start of the research study. This includes, but is not limited to, all independent undergraduate research projects and honors theses, masters' theses and dissertations. A faculty advisor/instructor signature is required as part of the submission process.

Recognizing the time constraints imposed on projects that must be completed within a single semester, the IRB will make every effort to work with faculty members/instructors to process proposals promptly. However, instructors must plan for and allow adequate time for the review process to occur (approximately two weeks to a month, depending on the particular human subject issues raised by the proposed research). The later in the semester a proposal is received, the more difficult it will be to accomplish the review in time for the projects to be completed during the current semester. It is very strongly urged that instructors require submission of IRB applications/protocols within the first



three weeks of the semester for projects that must be completed during the current semester.

Like all submissions to the IRB, student research projects will be reviewed on a rolling basis and may qualify for exempt or expedited review procedures if risks to subjects are no greater than minimal risk and meet other federal criteria. In the event the submission requires full review it will be placed on the agenda for the next available convened SBER IRB meeting. SBER IRB approval of a research protocol cannot be granted retroactively under any circumstances.

#### **11.17.1 Responsibilities of Faculty Advisors for all Student Conducted Research Projects**

Faculty advisors of both undergraduate and graduate students working with human subjects must be certified to conduct research with human subjects, even if they are not currently conducting research with human subjects. Certification to conduct research with human subjects is attained by completion of the CITI online tutorial. The certificate of completion for the tutorial must then be submitted to the IRB.

It is the responsibility of faculty advisors to determine when an undergraduate or graduate student project meets the definition of research. The IRB office will assist the faculty in making such determination. If the project is defined as human subject research, an IRB approval for the project is required.

Faculty members are also responsible for the review and approval of the scientific integrity of the proposed research project, including assessing the scientific rigor and merit of a study.

Faculty are responsible to ensure that a final report is submitted when the project is complete. If final reports are not submitted, the faculty advisor will not be able to receive approval for a new study until a final report is submitted for a project that has been completed.

#### **11.17.2 Responsibilities of Student(s) Investigators in Conducting Research**

- A. Undergraduate and graduate students working with human subjects must be trained to conduct research with human subjects. Certification to conduct research with human subjects is attained by completion of the CITI online tutorial. Completion of training is automatically recorded and reported to IRB.
- B. The investigator(s) has primary responsibility for protecting the rights and welfare of human research subjects and for complying with all applicable provisions of Institution's Federal Wide Assurance (FWA).
- C. The investigator(s) conducts all research according to Institutional Review Board (IRB) approved protocol and complies with all IRB determinations.
- D. The investigator(s) does not initiate any changes without IRB review and approval, unless it is necessary to eliminate an immediate hazard. Changes can

include, but are not limited to, the following examples: changes in principal investigator, in approved number of participants, in procedures or methods, in recruitment methods or materials. [Click here](#) for a copy of the Request for Protocol Modification form.

- E. The investigator(s) ensures that all researchers in the study have the appropriate training and comply with IRB approved conduct for the research.
- F. The investigator(s) ensures each potential subject understands the nature of research.
- G. The investigator(s) provides a copy of the IRB approved consent document to each subject, unless waived by the IRB.
- H. The investigator(s) retains (in the manner specified in the protocol) all signed consent documents and research evidence for at least 7 years beyond the completion of the research.
- I. The investigator(s) retains (in the manner specified in the protocol) all submission documents with signatures, all approval documentation, including signed approval letter, stamped interview/survey/questionnaire protocols, and all approved modifications for at least 7 years beyond the completion of the research.
- J. The investigator(s) reports progress to the IRB annually through continuing review or earlier (if required by the IRB) if recruitment of subjects, data collection, or contact with subjects will continue.
- K. The investigator(s) promptly reports any unanticipated problems to the IRB.
- L. Student researchers must work closely with faculty advisors to close the study when the project comes to an end. If the study is not closed, faculty advisor may take appropriate action on student researcher.

## **ARTICLE 12: SOCIAL BEHAVIORAL AND EDUCATIONAL RESEARCH (SBER) IRB**

### **12.1 Social, Behavioral and Educational IRB Designation**

The Institution does not have a designated Social, behavioral and Educational (SBER) IRB. All Institution's IRBs shall review all social and behavioral research involving human subjects for compliance with federally mandated research guidelines.

Research in SBER involves the study of humans at the level of the individual, small group, institution, organization, community, or population. At the individual level, this research may involve the study of behavioral factors such as cognition, memory, language, perception, personality, emotion, motivation, and others. At higher levels of aggregation, it includes the study of social variables such as the structure and dynamics of small groups (e.g., couples, families, work groups, etc.); institutions and organizations (e.g., schools, religious organizations, etc.); communities (defined by geography or common interest); and larger demographic, political, economic, and cultural systems. Research on social and behavioral processes also includes the study of the interactions within and between these two levels of aggregation, such as the influence of socio-cultural factors on cognitive processes or emotional responses. Finally, this research also includes the study of environmental factors (both natural and human created) such as climate, noise, environmental hazards, residential and other built environments and their effects on social and behavioral functioning.

IRB Protocol submission for Social, Behavioral and Educational requires submission of a specific protocol using the protocol template named "Protocol Template for SBER", which is available in the following link:

<https://research.rowan.edu/officeofresearch/compliance/irb/submissions/initialsubmissions/index.html#A1>.

The IRB shall review the following research categories:

- A. Experimental non-medical research (cognitive, behavioral, group, etc.);
- B. Minimal risk studies conducted in public or private settings, innocuous to varying behavioral modifications and interventions which do not cause physical harm;
- C. Archival research/non-medical record reviews and educational records;
- D. Survey/questionnaire research (in person and/or over the phone);
- E. Observational research (may or may not be covert, but observer may not be a participant);
- F. Research interviews;
- G. Oral histories (non-human subject research designation);
- H. Educational research;
- I. Epidemiological research using only social-behavioral methodologies;
- J. Some studies evaluating heredity and human behavior, disasters and human behavior, genetics, race and IQ, psychobiology and sociobiology and
- K. Pedagogical and methodological research.

The IRB will evaluate risks in social behavioral research risk may be less predictable, more subjective and variable and less remedial than other harms. In SBER, research risk may be presented as social harm, harming the reputation of the participant, disruption of personal and family relationship, privacy and confidentiality. Psychological harm when deception is involved.

The IRB will determine whether the deception is necessary and when necessary how participants are debriefed. IRB may consider that de-briefing itself may present an unreasonable harm without countervailing benefit. However, IRB will be aware that in some research if subjects are told about the research design and the purpose in advance, it may not be possible to conduct such research. Thus, IRB will take reasonable standards to protect participants.

In social, behavioral and educational research review, IRB will review the possibility of moral wrong such as ethical problems posed by deception, invasion of participants privacy, embarrassment or stigma and group stereotyping.

Other forms of risk may include financial harm, legal harm and political harm. In all cases, the IRB will take reasonable standards and appropriate measures to protect participants.

While reviewing certain behavioral research, ethical debates may ensue out of the fear that some sensitive data may be used to justify social stratification and prejudice. The possible use/misuse of such data will NOT be a matter for IRB review.

If the investigator is unsure whether the activity being planned to conduct is human subject's research, the investigator should contact the IRB office for assistance. Once a joint determination is made (investigator and IRB office), the investigator must submit an CIRB application by designating "non-human subject research as the review status at the time of submission. The IRB Chair/IRB Director shall review the protocol and sign a non-human subject determination letter. If non-subject determination leads to IRB review, then the investigator must submit either exempt or expedited review application. It is very rare that such applications would require a full board review.



## **ARTICLE 13 - ONGOING RESPONSIBILITIES FOLLOWING IRB APPROVAL**

### **13.1 Reporting Adverse Experiences**

Guidelines on reporting adverse events are described in Article 7.

#### **13.1.1 Definition**

An "adverse experience" or event is any occurrence, whether or not anticipated or expected, that causes a serious adverse effect on the health, safety, or welfare of the subject. It includes, but is not limited to:

- A. Any life-threatening problems caused by or associated with the subject's participation in the research;
- B. Any experience that suggests a significant hazard, contraindication, side effect, or need for precaution associated with the test article and its use;
- C. Any experience in the research that is permanently disabling;
- D. Any experience in the research that requires unplanned inpatient hospitalization;
- E. Any experience in the research that results in a congenital anomaly, cancer, or overdosing of an approved drug and
- F. Adverse experiences may also occur in Social and Behavioral Research

#### **13.1.2 Importance**

Prompt, full, and accurate reporting of unanticipated adverse experiences involving risks to research subjects and others is a major responsibility of investigators. Reporting of unanticipated adverse events is intended to prevent unnecessary harm to other current and future research subjects and to provide to the manufacturer, the FDA, and the IRB information to make decisions about the research that is under way, such as whether the anticipated risk-benefit ratio has changed. Newly discovered, including unanticipated, risks also may necessitate revising the informed consent.

#### **13.1.3 Reporting Requirements (HHS)**

Common Rule requires unanticipated adverse experiences must be promptly reported so that appropriate steps are taken in a timely manner to protect other subjects from avoidable harm. For example, an unanticipated problem that resulted in a subject's death or was potentially life-threatening generally should be reported to the IRB within a shorter time frame than other unanticipated problems that were not life-threatening.

- A. Unanticipated problems that are serious adverse events should be reported to the IRB within 1 week of the investigator becoming aware of the event.
- B. Any other unanticipated problem should be reported to the IRB within 2 weeks of the investigator becoming aware of the problem.
- C. All unanticipated problems should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the

supporting agency head (or designee), and OHRP within one month of the IRB's receipt of the report of the problem from the investigator.

In some cases, the requirements for prompt reporting may be met by submitting a preliminary report to the IRB, appropriate institutional officials, the supporting HHS agency head (or designee), and OHRP, with a follow-up report submitted to the IRB at a later date when more information is available. Determining the appropriate time frame for reporting a particular unanticipated problem requires careful judgment by persons knowledgeable about human subject protections. The primary consideration in making these judgments is the need to take timely action to prevent avoidable harms to other subjects. If investigators have any questions on reporting adverse events in projects funded by HHS, they must contact the IRB office for guidance.

#### **13.1.4 Determining and Reporting Requirements in Clinical Trials of Drugs and Biological Products**

According to FDA an unexpected adverse drug experience is defined as “[a]ny adverse drug experience, the specificity or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the investigator brochure only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the investigator brochure only listed cerebral vascular accidents. Unexpected, as used in this definition, refers to an adverse drug experience that has not been previously observed (e.g., included in the investigator brochure), rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product.” (21 CFR 312.32(a)) unanticipated problem involving risk to human subjects. FDA recommends that a discussion of the divergence from the expected specificity or severity accompany the report.

FDA also recommends that there be careful consideration of whether an AE is an unanticipated problem that must be reported to IRBs. In summary, FDA believes that only the following AEs should be considered as unanticipated problems that must be reported to the IRB.

A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure (such as angioedema, agranulocytosis, hepatic injury, or Stevens-Johnson syndrome).

A single occurrence, or more often a small number of occurrences of a serious, unexpected event that is not commonly associated with drug exposure, but uncommon in the study population (e.g., tendon rupture, progressive multifocal leukoencephalopathy).

Multiple occurrences of an AE that, based on an aggregate analysis, is determined to be an unanticipated problem. There should be a determination that the series of AEs represents a signal that the AEs were not just isolated occurrences and involve risk to human subjects (e.g., a comparison of rates across treatment groups reveal higher rate in the drug treatment arm versus a control). We recommend that a summary and analyses supporting the determination accompany the report.

An AE that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations. For example, if transaminase elevation is listed in the investigator's brochure and hepatic necrosis is observed in study subjects, hepatic necrosis would be considered an AE.

A serious AE that is described or addressed in the investigator's brochure, protocol, or informed consent documents, but for which the rate of occurrence in the study represents a clinically significant increase in the expected rate of occurrence (ordinarily, reporting would only be triggered if there were a credible baseline rate for comparison). We recommend that a discussion of the divergence from the expected rate accompany the report.

Any other AE or safety finding (e.g., based on animal or epidemiologic data) that would cause the sponsor to modify the investigator's brochure, study protocol, or informed consent documents, or would prompt other action by the IRB to ensure the protection of human subjects. We recommend that an explanation of the conclusion accompany the report.

For research in which FDA reporting is not required, adverse experiences, must be reported to the IRB within five working days, or earlier if required by the sponsor. The PI must also submit to the IRB, within five working days from date of submission, copies of any reports of unanticipated adverse experiences submitted to the sponsor, FDA, or any other organization, agency or individual that describes the clinical management of the adverse experience.

The PI must also submit through CIRB any unanticipated adverse experience reports that may have occurred at other investigative centers, reported by the sponsor, within five working days of their receipt. With each Adverse Event Report that is submitted to the IRB, the PI must also attach a completed Adverse Event Report form (whether the AE is on-site or off-site) and a copy of the



currently approved (date-stamped) consent form. If the PI feels that the adverse event requires a change to the consent form, a copy should be submitted with the changes highlighted (with yellow highlighter or distinctive typeface. A clean copy of the consent form changes must also be submitted for date-stamping).

### **13.1.5 Determining and Reporting Requirements in Clinical Trials of Devices**

The investigational device exemption (IDE) regulations define an unanticipated adverse device effect (UADE) as “any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects” (21 CFR 812.3(s)). UADEs must be reported by the clinical investigator to the sponsor and the reviewing IRB, as described below:

- A. For device studies, investigators are required to submit a report of a UADE to the sponsor and the reviewing IRB as soon as possible, but in no event later than 10 working days after the investigator first learns of the event (§ 812.150(a)(1)).
- B. Sponsors must immediately conduct an evaluation of a UADE and must report the results of the evaluation to FDA, all reviewing IRBs, and participating investigators within 10 working days after the sponsor first receives notice of the effect (§§ 812.46(b), 812.150(b)(1)).

The IDE regulations, therefore, require sponsors to submit reports to IRBs in a manner consistent with the recommendations made above for the reporting of unanticipated problems under the IND regulations.

### **13.1.6 Reporting Unanticipated Problems to IRBs**

An investigator participating in a multicenter study may rely on the sponsor’s assessment and provide to the IRB a report of the unanticipated problem prepared by the sponsor. In addition, if the investigator knows that the sponsor has reported the unanticipated problem directly to the IRB, because the investigator, sponsor, and IRB made an explicit agreement for the sponsor to report directly to the IRB,<sup>8</sup> and because the investigator was copied on the report from the sponsor to the IRB, FDA intends to exercise its enforcement discretion and would not expect an investigator to provide the IRB with a duplicate copy of the report received from the sponsor.

### **13.1.7 Reporting Requirements (FDA)**

Unanticipated adverse experiences must be reported within the required time periods. In each instance, a copy of the PI’s FDA/sponsor report must be submitted to the IRB within three working days of the required external report.

For research in which FDA reporting is not required, adverse experiences, must be reported to the IRB within five working days, or earlier if required by the sponsor. The PI must also submit to the IRB, within five working days from date of submission, copies of any reports of unanticipated adverse experiences submitted to the sponsor, FDA, or any other organization, agency or individual that describes the clinical management of the adverse experience.

The PI must also submit through CIRB any unanticipated adverse experience reports that may have occurred at other investigative centers, reported by the sponsor, within five working days of their receipt. With each Adverse Event Report that is submitted to the IRB, the PI must also attach a completed Adverse Event Report form (whether the AE is on-site or off-site) and a copy of the currently approved (date-stamped) consent form. If the PI feels that the adverse event requires a change to the consent form, a copy should be submitted with the changes highlighted (with yellow highlighter or distinctive typeface. A clean copy of the consent form changes must also be submitted for date-stamping).

#### **13.1.8 Failure to Comply**

When a PI fails to comply with any of the requirements, a letter from the IRB will initially warn the PI, with copies to the PI's department Chair and the IO. A second violation will result in a letter to the study's sponsor. After further violations, research may be suspended or terminated by the IRB in accordance with Article 4.10.6 of these Guidelines. The PI may be subject to disciplinary action pursuant to appropriate Institution policies and, if applicable, medical staff policies and bylaws.

#### **13.2 IRB Responsibilities to Review Adverse Events**

Investigators should follow the Unanticipated Problems – Adverse Events guidance on the IRB website at <https://sites.rowan.edu/officeofresearch/compliance/irb/index.html> to determine if an adverse event must be reported to the IRB.

When adverse events are submitted through CIRB, the IRB Director or IRB Chair will conduct the initial review. They will then assign an IRB member with appropriate expertise to conduct the initial review. The adverse event will also be reported by the Chair or IRB Director to the IRB. The reviewer will report the findings to the IRB for further action. The action may include asking further detailed information on the event or suggest modifications to the protocol and the consent form or approve the adverse event with no further changes to the protocol. If modifications are required, the IRB will notify the investigator to modify the protocol and the consent form and may require the investigator to re-consent those participants who have already been enrolled. If the proposed change necessitates a modification in the consent form, a revised consent form should be attached to this submission for IRB approval

### **13.3 Study Closures**

The completion or termination of a research protocol is a change in activity and must be reported to the IRB. A final report to the IRB allows the closure of all files as well as providing information that may be used by the IRB in the evaluation and approval of related studies. When a study is closed, no further research, follow-up or data analyses will be performed. If any subjects are ongoing, the study may not be closed. A study is not closed simply because no additional subjects will be enrolled.

To close a study in CIRB, the investigator must submit a continuing review form. When filling out the form, in the study status section, select "Final Report".

#### **13.3.1 Failure to Close the Study**

After the final report is submitted, the report will undergo review by the IRB. The IRB may request additional information to ensure that the study is in good standing and ready to be closed. Once the submission is approved, the study is considered "Closed" by the IRB. If an investigator wishes to resume the research after it has been closed, a new study will have to be submitted. Failure to close the study when the project is ended may result in additional IRB action which includes no new IRB applications to be approved until a completed study has been closed by submitting a final report.

Once a study has been completed, investigators may keep the data they collected, including identifiable private data, if consistent with the IRB-approved research plan. Investigators should continue to honor any confidentiality protections of the data. Investigators also should honor any other commitments that were agreed to as part of the approved research, for example, providing information about the study results to research subjects, or honoring commitments for compensation to research subjects for research participation.

If a study is in data analysis phase, the investigator must submit a final report indicating that the study is in data analysis phase. Studies in data analysis phase do not require annual continuing review or progress report.

## **ARTICLE 14 - GENETIC TESTING**

### **14.1 Genetic Testing Requirements**

Genetic research does not mean only research that involves looking for mutations in DNA. Research that involves looking at the differences between proteins in individuals with or without a certain disease can also qualify as genetic research. Records research involving information that was derived from a previous genetic test can also qualify as genetic research. See definitions below. If genetic testing to be done on biospecimens collected as part of broad consent, the donors must be given an option to agree to use their specimen for genetic testing or donors should be made aware on the broad consent that the person collecting the biospecimen is unaware how the donor's specimen that has been collected and stored will be used in the future.

- A. Genetic research: Research using human DNA samples, genetic testing or genetic information.
- B. Genetic information: Information about an individual or the individual's blood relatives obtained from a genetic test.
- C. Genetic test: A test for determining the presence or absence of genetic characteristics in a human individual or the individual's blood relatives, including tests of nucleic acids, such as DNA, RNA, and mitochondrial DNA, chromosomes or proteins in order to diagnose or determine a genetic characteristic.
- D. Genetic characteristic: A gene, chromosome or alteration thereof that may be tested to determine the existence of or risk for acquiring a disease, disorder, trait, propensity or syndrome, or to identify an individual or a blood relative. "Genetic characteristic" does not include family history or a genetically transmitted characteristic whose existence or identity is determined by means other than through a genetic test.

### **14.2 Special Considerations for Anonymous and Coded Genetic Research**

- A. Investigators proposing to conduct coded or anonymous genetic research must submit the project for review by the IRB.
- B. When an investigator wishes to conduct genetic research using biological specimens or information from patients or subjects and does not have informed consent for the use of anonymous or coded biological specimens or information in the specific genetic research project, the following requirements must be met:
  - a. The individual(s) from whom the biological specimen(s) or information will be or has been obtained must have been provided with the "Notice of Your Right to Refuse Participation in Future Anonymous and/or Coded Genetic Research" and did not exercise his/her right to refuse to participate in coded or anonymous genetic research (opt out), as verified by appropriate genetic opt out review or
  - b. The individual(s) from whom the biological specimen(s) or information will be or has been obtained has granted consent for genetic research generally or

- c. The individual(s) from whom biological specimen(s) or information will be obtained is deceased (or specimen or information was obtained in emergency circumstances but the individual died before receiving opt out notice) or
- d. The biological specimen(s) or information was obtained prior to July 29, 2005.
- e. If the specimen(s) or information are coded, the following additional requirements apply:
  - i) The code is:
    - (a) Not derived from individual identifiers;
    - (b) Kept securely and separately from the specimens and information; and
    - (c) Not accessible to the investigator unless specifically approved by the IRB.
  - ii) The information is stored securely in password protected electronic files or by other means with access limited to authorized personnel.
  - iii) The information is limited to elements required for analysis and meets the criteria in **45 C.F.R 164.514(e)** for a limited data set.

The IRB shall determine whether proposed genetic tests pose risks to individuals participating in a study regardless of the funding source. The IRB will require that the consent form shall inform subjects that:

- A. They have been asked to participate in a research study in which their blood or other tissue samples are used for genetic testing;
- B. Subjects will have an option not to participate in the study;
- C. Subjects will have an option to withdraw from the study;
- D. Subjects will have the option for receiving results of the study, disclosing test results to their relatives or their doctor and
- E. Whenever genetic testing or genetic information is obtained from participants, such studies should include the GINA language on the consent form.

## ARTICLE 15 – HIPAA

### 15.1 HIPAA (Health Insurance Portability and Accountability Act)

On April 14, 2003, HIPAA rules came into effect. Under this rule, researchers working at RowanSOM are permitted to use and disclose PHI (Protected Health Information) for research with individual authorization, or waiver of authorization as set forth in the HIPAA Privacy Rule.

In clinical research, physician-investigators often stand in dual roles to the subject as a treating physician and as a researcher. For the treating physician, duties of confidentiality have long been established under well-known legal and ethical standards. The Privacy Rule adds to these existing obligations. Where a covered entity conducts clinical research involving protected health information (PHI), physician-investigators need to understand the Privacy Rule's restrictions on the use and disclosure of PHI for research purposes. As the Federal privacy standards are implemented throughout the country, one benefit is that many clinical researchers and hospitals may adhere to a common set of national standards for protecting the privacy of patients and clinical research subjects.

The fact sheet published by the NIH ([http://privacyruleandresearch.nih.gov/clin\\_research.asp](http://privacyruleandresearch.nih.gov/clin_research.asp).) discusses the Privacy Rule and its impact on covered entities that conduct clinical research. It places specific emphasis on the Authorization that is generally required for research use and disclosures of PHI by covered entities.

### 15.2 HIPAA Training

Every employee and students at Rowan SOM must complete HIPAA Compliance training (**OCCI103**). This training is available in the following link: <https://www.rowan.edu/compliance/>.

Investigators conducting medical research at all campuses who use protected health information must complete HIPAA Privacy and Security Medical Research Compliance Training **OCCI1103 and OCCI109**.

For additional information on HIPAA training, contact Rowan SOM at 856-566-6229 or 856-566-6136.

### 15.3 List of HIPAA Identifiers

The following identifiers of the individual or of relatives, employers, or household members of the individual, are considered PHI identifiers under HIPAA:

1. Names
2. Postal address  
All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial

three digits of a zip code if, according to the current publicly available data from the Bureau of the Census:

(1) The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and

(2) The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people are changed to 000.

3. Dates

All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older;

4. Telephone numbers

5. Fax numbers

6. Electronic mail address

7. Social security numbers

8. Medical record numbers

9. Account numbers

10. Health plan beneficiary number

11. Certification/license numbers

12. Vehicle identifiers and serial numbers, including license plate numbers

13. Device identifiers and serial numbers

14. Name of relative

15. Web Universal Resource Locator (URL)

16. Internet Protocol (IP) address number

17. Biometric identifiers, including fingers and voice prints

18. Full face photographic images and any comparable images

*Any other unique identifying number, characteristic, or code*

#### **15.4 Honest Broker**

The Privacy Rule (HIPAA) permits protected health information (PHI) to be used without patient authorization in a number of limited circumstances such as the use of de-identified PHI. PHI can either be de-identified by an honest broker, who is a member of the covered entity (RowanSOM) or by an honest broker that is a business associate of the covered entity.

An honest broker is an individual, organization or system acting for, or on behalf of, the covered entity to collect and provide health information to research investigators in such a manner whereby it would not be reasonably possible for the investigators or others to identify the corresponding patients/participants directly or indirectly. The honest broker cannot be one of the investigators. The information provided to the investigators by the honest broker may incorporate linkage codes to permit information collation and/or subsequent inquiries (i.e., a “re-identification code”), however the information linking this re-identification code to the patient’s identity must be retained by the honest broker and subsequent inquiries are conducted through the honest broker.

### **15.5 Preparatory to Research**

Preparatory to research representation provision permits covered entities to use or disclose protected health information for the purpose of developing a research protocol, formulating a research hypothesis, or screen for study eligibility. See guidance for preparatory to research in the following link:

[https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1\\_27](https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1_27). However, the provision at 45 CFR

164.512(i)(1)(ii) does not permit the researcher to remove protected health information from the covered entity's site. As such, a researcher who is an employee or a member of the covered entity's workforce could use protected health information to contact prospective research subjects. The preparatory to research provision would allow such a researcher to identify prospective research participants for purposes of seeking their authorization to use or disclose protected health information for a research study.

Preparatory to research activities are defined as:

- A. The development of research questions;
- B. The determination of study feasibility (in terms of the available number and eligibility of potential study participants);
- C. The development of eligibility (inclusion and exclusion) criteria; and
- D. The determination of eligibility for study participation of individual potential subjects and
- E. The PHI used to identify prospective research participants could include contact information, diagnosis or condition, and other information necessary to determine study eligibility.

Although HIPAA considers the use and disclosure of PHI to determine study eligibility a preparatory to research activity, the actual process used to recruit subjects remains a research activity and requires IRB approval.

In order to receive approval for preparatory to research please complete the "Preparatory to Research Form" posted on the website

[https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1\\_27](https://sites.rowan.edu/officeofresearch/compliance/irb/policiesguidance/guidancelisting/preptoresearch.html#p7EPMc1_27).

### **15.6 Limited Data Set Agreement**

Limited data set (LDS) is an exemption to the Privacy Rule requirement for an authorization from the subject for research use of protected health information (PHI). LDS lacks 16 of the 18 identifiers listed above (Section 15.2). LDS may contain dates of birth, date of death, dates of service, town or city, state or zip code. If you are using the dates and zip codes, you must obtain a limited data set agreement. For further information of obtaining LDS agreement, please contact the Office of Compliance, RowanSOM at 856-566-6136 or email at [braeunrc@rowan.edu](mailto:braeunrc@rowan.edu).



### **15.7 Data Use Agreement**

A Data Use Agreement (DUA) is a contractual document used for the transfer of data that has been developed by nonprofit, government or private industry, where the data is nonpublic or is otherwise subject to some restrictions of its use. Often this data is a necessary component of a research project and it may or may not be human subject data from a clinical trial, or limited data set information as defined in HIPAA. The Institution wants to ensure that DUA terms protect confidentiality when necessary, but permit appropriate publication and sharing of research results in accordance with institution policies, applicable laws and regulations, and federal requirements. DUAs are similar to confidentiality agreements, and, in some cases, a CDA (confidentiality disclosure agreement) format may be used to transfer data. If data transfer is part of a larger agreement between institutions where in PHI is NOT part of the data that will be transferred, but they are part of a funding agreement (grant, contract, sub-award, contracted services agreement, etc.) in those cases, a separate DUA is not necessary.

All DUAs are reviewed by the general counsel's office. DUAs should not be signed by Institution's faculty or staff members and it is signed by the individual authorized to sign on behalf of the Institution.

### **15.8 Decedent Health Information**

Use of decedent health information requires (1) the researcher seeking access to decedent's PHI must obtain permission from the IRB indicating in a memo that the use and disclosure is sought solely for research on the PHI of decedents; (2) the memo indicating that the PHI for which use or disclosure is sought is necessary for the research purposes, and (3) documentation, at the request of the covered entity, of the death of the individuals whose PHI is sought by the researchers. For further information of obtaining LDS agreement, please contact the Office of Research Compliance, RowanSOM.

## ARTICLE 16 – CASE REPORTS AND CASE STUDIES

### 16.1 Case Reports

Generally they consist of three or fewer patients and are prepared for the purpose of illustrating some points in the care of a patient, to educate and formulate new research questions which may eventually lead to generalizable knowledge.

- A. Uncommon observations
- B. Report of a new condition, treatment and follow up
- C. Report of a familial condition with a proposed mode of inheritance
- D. A new theory
- E. Questions regarding a new theory
- F. Unusual combination of conditions or events that cause confusion
- G. Adverse responses to therapies
- H. Personal Impact
- I. In addition, case reports may include:
  - 1. Very common observations or practices that has not been documented previously
  - 2. Unique aspects of the practice such as outreach and engagement into care, case management and collaborations, clinical adaptations to care
  - 3. The competing priorities of patients while homeless and how care needs to accommodate them.

This policy is developed to provide guidance on when publication of case reports constitute human subject research and review by IRB.

### 16.2 Guidance on Medical Case Reporting

The boundaries between case reporting and formal medical records research may be unclear for a series of one's own patients. Researchers are advised to consult with the IRB when uncertainty exists and when formal and systematic collection of human subject's research is/will be occurring.

The Federal regulations for the Protection of Human Subjects (**45 CFR 46.102(d)**) defines "research" as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. In general, the reviews of medical records for publication of "case reports" typically involve three or less patients. In such circumstances, they are NOT considered human subject research and may not require IRB review since they do not formulate research hypothesis.

Formal retrospective or prospective medical records review involving larger patient population [greater than three (3) subjects] are subject to either exempt (if data is existing and anonymous) or expedited IRB review with subject's consent and authorization or waiver of consent and waiver of authorization. This is because, in these circumstances, researchers are beginning to ask questions and collect data either prospectively or retrospectively to systematically analyze data making the study closer to deriving generalizable knowledge.

### **16.3 Case Studies**

This is generally applicable to social, behavioral and educational scientists. It is the in-depth analysis, empirical inquiry, or investigation of a person or group in a natural, uncontrolled setting. This research method is done from the participants' perspective not how researchers manipulate it. Qualitative researchers study things in their natural settings, attempting to make sense of, or to interpret, phenomena in terms of the meanings people bring to them.

Case study research can mean single and multiple case studies, can include quantitative evidence, relies on multiple sources of evidence, and benefits from the prior development of theoretical propositions. Case studies should not be confused with qualitative research and they can be based on any mix of quantitative and qualitative evidence. Single-subject research provides the statistical framework for making inferences from quantitative case-study data.

### **16.4 Policy on Case Studies**

This is generally applicable to social, behavioral and educational scientists. Case studies include multiple data sources such as interviews, documents, archival records, direct observations, and physical artifacts. Analysis is through description, themes, and assertions. Researchers from many disciplines (e.g., social/behavioral, educational, epidemiological) use this method to build upon, produce new, and dispute current theory.

A single retrospective case study that reports the observation of a single subject receiving the normal standard of care (no new or novel procedures) is generally not considered research since it does not meet the definition of systematic investigation leading to generalizable knowledge. However, many researchers in the social sciences fields believe that this when a series (more than one) of subject observations is compiled in such a manner that would allow possible extrapolation of the results to a larger population, this would likely represent research. If identifiers are recorded in a multi case study, if data manipulation is part of the research objective or the data is relating to special population, investigators are directed to submit an expedited or full board application. If the study is a single case study, case series of chart review, investigators are directed to submit an exempt review application.

The decision if a prospective case study that includes experimental intervention (even if "n = one", if identifiers are collected, includes special population and if incentives are offered, investigators are directed to submit an expedited or full board review application. Please contact the IRB office before submitting an application. If the case study does not involve any of the items discussed in this paragraph, investigators are directed to submit a non-humans subject research application.

### **16.5 Confidentiality in Case Reports and Case Studies**

Participant's bill of rights to confidentiality must always be respected when using their personal or medical information. Please pay particular attention to the following when attempting to publish a case report:

- A. Patient's 18 HIPAA identifiers noted in HIPAA regulations or combinations of those identifiers, which might easily allow someone to identify a subject, should never be used in publications or presentations. In cases where HIPAA identifiers are not used, investigator must specify that the data will be anonymous and there will be no link to the patient charts;
- B. If link to chart is going to be kept, a consent and authorization from the subject may be required or the investigator may request for a waiver of consent and authorization to the IRB/Privacy Board. The IRB shall make the final decision on granting the waiver of authorization;
- C. In reports containing familial condition with a proposed mode of inheritance, unique family trees or pedigrees should be masked or disguised in the publication when such information could identify individuals or kindreds unless a consent/permission has obtained from those subjects;
- D. When photographs or other images are going to be used in the publication, identifiers should be appropriately masked to preclude identification of subjects; In some cases, patient's permission may be necessary to publish such case reports.
- E. Investigators should be sensitive to the unique or unusual diagnoses or illnesses, which when combined with the hospital name, state or city of residence might identify a subject with such rare diagnosis when published in research papers or text books and
- F. Investigators must abstract and retain only the minimum relevant clinical information. Investigators must not retain the links indefinitely. They must discard links to human subjects as soon as the research goals have been met and data analysis has been completed and published.

