ROSALIND FRANKLIN UNIVERSITY of MEDICINE AND SCIENCE

POLICY MANUAL

Institutional Review Board

for the

Protection of Human Subjects Research

This document is applicable for human subject research covered by the

"Final Rule" or "Revised Common Rule"

that went into effect January 21, 2019

Citations in the manual refer to the U.S. Department of Health and Human Services (HHS) regulations at 45 CFR 46, Subpart A as published in the Federal Register January 19, 2017.

Update: 8-9-22

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I. INTRODUCTION

A. <u>Authority and Responsibility Delegated to Executive Vice President for Research</u>.
The President and CEO of Rosalind Franklin University has designated the Executive Vice President for Research as the Institutional Official with authority and responsibility to develop, implement and oversee policies, procedures, and practices in order to ensure compliance with and promote the policy that:

> ***All activities relating to the conduct and oversight of human subject research conducted under the auspices of Rosalind Franklin University shall be in compliance with applicable laws and ethical principles, the Federal Wide Assurance (FWA), and relevant University policies and procedures, and shall be conducted in a manner that protects the rights and welfare of the human subjects involved in that research. Violations of this policy are prohibited and could result in sanctions, including termination*** *(See also: Appendix A).*
>
> Key definitions of terms in the policy are presented here:
>
> 1. The term **"human subject",** as it relates to research, means a living individual about whom an investigator (whether professional or student) conducting research: (i) Obtains information or biospecimens through *intervention* or *interaction* with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates *identifiable private information* or *identifiable biospecimens*.
>
> *Intervention* includes 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.
>
> *Interaction* includes communication or interpersonal contact between investigator and subject.
>
> *Private information* includes 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).
>
> *Identifiable private information* is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
>
> An *identifiable biospecimen* is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.
>
> *NOTE: For research subject to **FDA regulation**, the definition of "human subject" is an individual who is or becomes a human subject in research, either as a recipient of the test article or as a control. A human subject may be a healthy individual or a patient.*

2. The term **"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.

For purposes of this part, the following activities are deemed not to be research:

(1) 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.

(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

*NOTE: For research subject to **FDA regulation**, the definition differs. The FDA definition of research (also known as "clinical research, clinical study, study, or clinical investigation") is: Any experiment that involves a test article and one or more human subjects, and that either:*

** must meet the requirements for prior submission to the FDA (i.e. any use of a drug other than use of an approved drug in the course of medical practice OR any activity that evaluates the safety or effectiveness of a medical device) OR*

** need not meet the requirements for prior submission to the FDA, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.*

3. The phrase "**conducted under the auspices of the University**" as it relates to research means research in which a University employee or agent, for the purposes of the research project, (i) Obtains information or biospecimens through intervention or interaction with the individual, or uses, studies, or analyzes the information or biospecimens; (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens; or (iii) Participates in recruitment of or the

process of obtaining the informed consent of human subjects for the research. The term "**engaged in the research**" in reference to the University or a University employee or agent is also used in this manual to denote human subjects research that is conducted under the auspices of the University.

*NOTE: "**University employee or agent**" means any individual who: (1) acts on behalf of the University; (2) exercises University authority or responsibility; or (3) performs University designated activities. "**Employee or agent**" can include faculty, staff, students, contractors, and volunteers, and others, regardless of whether the individual is receiving compensation from the University.*

4. The "**applicable laws**" include The Common Rule (one version of which is codified at 45 C.F.R. Part 46) and the FDA regulations (codified at 21 C.F.R. Parts 50, 56, 312, 812, and 814). In addition, several state laws and/or tribal laws passed by the official governing body of an American Indian or Alaska Native tribe may be applicable, depending upon the specifics of the research project. The applicable ethical principles include those set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. In addition, international organizations have developed ethical guidance documents, which may at times be applicable.

B. This Manual. In accordance with that delegated authority described in Appendix A, the Executive Vice President for Research has implemented this Manual. All University employees and agents (which includes all faculty, staff, students, contractors, and volunteers), are required to comply with this Manual, violations of which could result in sanctions, including termination.

C. Reporting Concerns and Non-Retaliation. Any person seeking guidance or who becomes aware of any potential, known, or suspected violation of this Manual shall report such matter to the Institutional Review Board (IRB) or, if the concern relates to the IRB, then to the Executive Vice President for Research, so that proper action may be taken. As an alternative, reports may be made to the Office of Compliance directly or through EthicsPoint, a NAVEX Global company, (which allows anonymity), either via its toll-free number (800-254-0460) or its URL (http://rosalindfranklin.ethicspoint.com). No person will be subjected to retaliation, retribution, or reprisal for making a good faith report of, seeking guidance regarding, or participating in the investigation or resolution of a potential, known, or suspected violation of this policy.

II. OVERVIEW OF THE IRB AND IRB STAFF

A. Introduction. The Institutional Review Board (IRB) is an administrative body established by the University to protect the rights and welfare of human subjects recruited to participate in research conducted under the auspices of the University. The IRB exercises authority as described in this Manual and functions independently from, but in coordination with, other committees and boards of the University. No person may attempt to unduly influence any member of the IRB or its staff.

B. Composition. The Executive Vice President for Research will appoint, in writing, IRB members from varying backgrounds and sufficient levels of experience and expertise to promote complete and adequate review of research activities commonly conducted by the University and give due consideration to those who would reflect diversity in race, gender, and cultural background and have sensitivity to community attitudes and vulnerable categories of research human subjects.

1. Membership consists of at least five members, that includes the following:

   a. At least three persons with University faculty appointments whose primary concerns are in scientific areas;
   b. At least one person whose primary concerns are in nonscientific areas;
   c. At least one person who is not otherwise affiliated with the University and who is not part of the immediate family of a person who is affiliated with the University;
   d. Other persons, when determined that their participation will promote the function of the IRB, such as:
      (i) persons knowledgeable in the areas of institutional policies, institutional resources, regulations, applicable law, and standards of professional conduct and practice; and
      (ii) persons knowledgeable about, experienced in working with, and sensitive to the special circumstances relating to vulnerable categories of research subjects commonly recruited in human subject research conducted under the auspices of the University, such as children, people who are incarcerated, individuals with impaired decision-making capacity, University students or employees, or economically or educationally disadvantaged persons,.

2. The Executive Vice President for Research will review and evaluate, at least annually, the IRB membership to determine whether modifications should be made. In the event modifications are made, the IRB staff shall notify the applicable government agencies (*e.g.* OHRP) of the updated IRB membership roster.

C. Chair and Vice Chair. The Executive Vice President for Research will select from the IRB membership, a person with appropriate character qualities and expertise in human subject research to perform the duties of IRB Chair and appoint, in writing, that person as Chair of the IRB. The Executive Vice President for Research will select from the IRB membership, using the same selection criteria used for the IRB Chair, and appoint in writing, one or two persons to serve as Vice Chair when the Chair is unavailable or needs recusal *(e.g. conflict of interest).*

D. Alternate Members. The Executive Vice President for Research may appoint, in writing, one or more alternate members to the IRB using the same criteria as used for selecting IRB members. An alternate member to the IRB may participate at an IRB meeting as a member in lieu of and during the absence of an IRB member, so long as the alternate's chief anticipated contribution to IRB deliberations is essentially the same as the absent IRB member's. For example, an alternate for an absent IRB member whose primary concerns are in nonscientific areas would be someone whose primary concerns are also in nonscientific areas; similarly, an alternate for an absent IRB member who is a science faculty member would be another science faculty member. All references in this Manual regarding requirements of IRB members apply as well to alternate members; all references in this Manual regarding authority of IRB members apply to alternate members when they are participating in lieu of and during the absence of an IRB member.

E. Education and Training. Members of the IRB and the IRB administrator are required to complete an initial education and training program before participating as an IRB member or administrator. The Human Subjects Research (HSR) Training is hosted on the CITI program website (citiprogram.org). All in-house IRB members and the IRB administrator are required to complete the CITI course for IRB Members; the community members of the IRB complete the IRB Community Member CITI course. The IRB Chair and Vice Chairs are required to complete the specific CITI modules for IRB Chair & Vice Chairs. Training must be renewed every three years. Additional training and education for IRB members and IRB staff will be as determined by the Executive Vice President for Research with the goal of providing information that promotes compliance with this Manual (*e.g*. attending the Public Responsibility in Medicine & Research (PRIMR) annual meeting). New information on the topic of Human Subject Research oversight considered important by the Executive Vice President for Research, the IRB Chair, or the IRB membership will also be disseminated to the IRB members on an ongoing basis (*e.g.* newly published government guidance or emerging ethical or scientific issues).

F. Conflict of Interest Disclosure Report. Before initial participation as an IRB member, and on an annual basis thereafter, each member of the IRB must complete and submit a conflict of interest disclosure report specifically tailored for IRB members that includes a description of the definition of conflict of interest as it pertains to IRB participation and reminds members of their continuing obligation to recuse themselves from reviewing a protocol with which they have a conflict of interest. These disclosure reports are to be forwarded to the IRB Office for retention.

> *NOTE: An IRB member will be deemed to have a "conflicting interest" with a particular research project when that person, their spouse, and/or dependent children either:*
> *1. has a personal interest that: a) will be affected by the research result, or b). is associated with the sponsor or a competitor of the sponsor; or*
> *2. is significantly involved in the design, conduct, or reporting of that research.*

G. Meetings of the IRB. When an IRB meeting is called, the following pertains:

1. Chair. The Chair of the IRB calls for meetings, controls the meeting agenda, and determines the appropriate times for all persons who are not eligible voting members to enter and depart the meeting.

2. Quorum. A quorum for the IRB exists when both of the following exist:

a. at least a majority of IRB members are present and qualified to participate; and
b. at least one member, whose primary concerns are in nonscientific areas, is present and qualified to participate.

NOTE: To determine the number for a "majority," only make reference to the IRB membership roster without alternates. Then, when counting the persons present, count all persons present including alternates. For example, if the IRB membership roster contains 12 names and the alternate IRB membership roster has 4 names, the number of persons who must be present for a majority is 7 (i.e. a majority of 12 is 7). Then, continuing with the same example, if 5 are present from the IRB membership roster and 2 are present from the alternate IRB membership roster, then there is a majority (i.e. 5 plus 2 equals 7, which is a majority in this example). To be "present" includes participating through the use of communications equipment wherein all participants can communicate with each other contemporaneously. Voting by proxy is not permitted. To be "qualified to participate" means the member present is current in the education and training requirement, current in the conflict of interest disclosure report requirement, and has no conflicting interest in the particular protocol under review.

3. Opening Comments. The IRB Chair will open each meeting reminding the members that:

a. the University is committed to ethics and the protection of human subjects;
b. the function of the IRB body is to protect the rights and welfare of human subjects involved in human subject research, and
c. IRB members may not participate when they have a conflict of interest.

4. Presence of Guests.

a. Investigators. The presence of the Principal Investigator (PI) could be a useful source of information that enhances the review of a research project. Accordingly, the PI may be invited as a guest and is expected to appear at the IRB meeting to present matters as requested by the IRB and address concerns and questions of the IRB members. In the event the PI is invited but absent, the matter will be deferred until the next meeting unless the IRB determines (in its sole discretion) that either:
(1) an alternate representative of the research team is qualified and authorized to present matters and address the concerns and questions of the IRB, or
(2) the presence of the PI or an alternate representative is not necessary for a proper review.

b. Other Guests. The IRB Chair may invite other guests to the IRB meeting to provide information to the IRB as deemed appropriate by the IRB for a proper review. These guests may be individuals with competence in special areas to assist the IRB in its review of issues that require expertise beyond or in addition to that available on the IRB.

c. Departure of Guests. All guests will depart the meeting upon direction of the IRB Chair and normally no guest will be present during IRB deliberations and voting. Guests are not considered IRB members and do not vote.

d. Support Staff. Persons providing administrative or technical support to the IRB are not considered guests or members; the Chair may permit such support staff to remain throughout the IRB meeting.

5. Prior to Deliberations and Voting. Before the deliberation and vote:

a. Guests. The IRB Chair will determine whether any guest is permitted to remain (normally no guest will be present during IRB deliberations and voting). The following guests are required to depart prior to deliberations and voting:

(1) any guest who is an investigator or is in any other manner part of the research team of the research under review, and

(2) any guest whose presence compromises or appears to compromise the independence of the IRB or of any IRB member.

NOTE: The minutes shall reflect the departure of any guest that takes place prior to deliberation and voting.

b. IRB Member Conflict of Interest. The IRB Chair will ensure that no IRB member participates in the initial or continuing review activities of any project in which the member has a conflicting interest (except to provide information requested by the IRB) by ensuring that conflicted member departs the room prior to deliberations and voting and the IRB meeting minutes so reflect.

c. Quorum. The IRB Chair will verify whether a quorum remains, and if quorum is lost, that the IRB does not take action until the quorum is restored (unless the action is such that this Manual allows an IRB determination to be made without a meeting).

6. IRB Determination. The vote of a majority of members that are present and qualified to participate during a meeting in which a quorum exists is the determination of the IRB. A mere plurality, even in cases of a member or members abstaining, is not sufficient for an IRB determination. Only IRB members may vote. Voting by proxy is not permitted.

7. Minutes of Meeting. Written minutes for each meeting will be prepared and presented at the next meeting for approval. The minutes will contain at least the following information:

a. Date and time of the IRB meeting;

b. Names of members present with status to establish quorum;

c. Opening comments made;

d. For each research project reviewed for an approval decision:

(1) the number and title;

(2) names of guests present, their function, and material information provided;

(3) material issues raised during deliberations and how they were resolved;

(4) voting results for each IRB determination (number voting for, voting against, and abstaining) and whether quorum existed for the vote.

(5) whether the level of risk is minimal or more than minimal;

(6) whether a project is approved, conditionally approved, deferred with comments, or disapproved;
(7) the period for continuing review (*e.g.* one year or a time more or less than one year);
(8) other necessary factual findings, if any (*e.g.* those associated with waivers or vulnerable populations)
(9) whether all persons (guests and IRB members) with a conflicting interest departed the meeting before the deliberations and vote.

*NOTE: **"Material issues**" include the basis for requiring changes in research, the basis for disapproving research, a written summary of the discussion of controverted issues and their resolution, justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the informed consent document, and the rationale for risk determinations.*

e. For instances of providing information of recent IRB determinations made without a meeting (*e.g.* expedited review actions), a copy of the summary briefing sheet provided to the IRB that contains the relevant information described above in subparagraph II.G.7.d of this Manual.
f. For other IRB determinations (*e.g.* noncompliance-related determinations, suspension/termination of approval determinations), material information of similar significance as described above in subparagraph II.G.7.d of this Manual.

8. Records. The IRB minutes, copies of all documents reviewed or considered by the IRB during the meeting, records of other IRB oversight activities, and copies of relevant correspondence between the IRB and PIs will be maintained in the IRB Administration Office for a period of at least three years after completion of the research. Even when a protocol is terminated without human subject enrollment, the IRB records will be retained for at least three years after termination. Electronically scanned copies of paper documents may be used to fulfill this record retention requirement if they are accurate reproductions. IRB records will be made accessible for inspection and copying by authorized representatives of federal agencies or departments at reasonable times and in a reasonable manner.

H. IRB Staff. The IRB is administratively supported by the IRB staff, who shall report to and be supervised by, directly or indirectly, the Executive Vice President for Research. The IRB staff provides the following administrative support:

1. Maintain a current roster of IRB members (including alternate members, if applicable) that identifies each member by name, earned degrees, current licenses and certifications, affiliation status with the University, and information sufficient to document fulfillment the composition requirements contained in this Manual. In the event modifications are made, the IRB staff shall notify the applicable government agencies (*e.g.* OHRP) of the updated IRB membership roster.

2. Maintain a list of IRB members (including alternate members, if applicable) reflecting their current status regarding education and training and conflict of interest reports.

Notify the affected member and IRB Chair of approaching due dates and, when applicable, delinquency status.

3. Receive and process applications for IRB review, as further explained in this Manual; attend and prepare draft minutes of IRB meetings; prepare and deliver IRB correspondence, as requested; and brief the Executive Vice President for Research on IRB determinations as directed.

4. Maintain files of research projects reviewed by the IRB, which will contain the IRB minutes, copies of all documents reviewed or considered by the IRB, records of other IRB oversight activities, and copies of relevant correspondence between the IRB and PIs.

5. Send reminders to PIs about the need to apply for continuing protocol review in a timely manner (as further explained in Sections III and XI of this Manual), or to submit information concerning voluntary protocol closure (as further explained in Sections III and XI of this Manual), as applicable.
NOTE: Any failure of the IRB staff to fulfill this responsibility does <u>not</u> excuse the PI of their responsibility to comply with IRB requirements and the requirements of this Manual.

6. Receive information about concerns or requests, answer questions consistent with the Manual, provide assistance in locating information contained in this Manual, assist others seeking to obtain copies of this Manual and related government regulations, government guidance, and University guidance, forms, applications, and checklists.

7. Provide access to approved educational materials designed for human subjects; and receive information from potential, current, and past human subjects about their concerns or requests and forward that information to the IRB Chair.

8. Monitor relevant online resources, including the OHRP website, and other outlets for new information about IRB review and related issues; brief the IRB Chair about new information about IRB review and related issues and any recommended changes to this Manual based on that new information.

9. Maintain currency through continuing education and training and demonstration of knowledge of human subject research. Attend relevant conferences, as time and resources permit.

10. Ensure timely application and updates to OHRP regarding the University's Federal Wide Assurance (FWA) and Institutional Review Board (IRB) registration, including changes in IRB membership.

III. THE PRINCIPAL INVESTIGATOR

A. General Role and Responsibilities.

1. The Principal Investigator (PI) is the person with primary responsibility and accountability for the appropriate design, conduct, and reporting of the human subject research. A human subject research project conducted under the auspices of the University must have one and only one PI. Other investigators (i.e. those who share in the responsibility of the design, conduct, and/or reporting of human subject research) may exist.

2. To be designated as the PI of a human research project that will be conducted under the auspices of the University, the individual must:

a. Have a Rosalind Franklin University of Medicine and Science faculty appointment with the title of Professor, Associate Professor, Assistant Professor, or Instructor, regardless of suffix or prefix;
b. Have the experience, expertise, and skill sets appropriate for the particular research project; and
c. Accept and fulfill the responsibilities of the PI, as described below and elsewhere in this Manual.
d. If a faculty member who has a part-time or voluntary position with the University (*e.g.* clinician whose primary employment position is at a different institution), wishes to be PI on an IRB protocol at this University, prior authorization from the Executive Vice President for Research and a formal written IRB agreement will be required.

B. Specific Responsibilities of the PI.

1. Ensuring that no human subject research is initiated until approval or a determination of exempt status is obtained from the IRB and that necessary resources are present.

2. Once IRB approval has been obtained, ensuring that human subject research is conducted in accordance with applicable laws and ethical principles, in accordance with this Manual and other relevant University policies and procedures, in accordance with IRB requirements, and in a manner that protects the rights and welfare of the human subjects involved in that research.

3. Ensuring that no changes or modifications, however minor, to the human subject research (*e.g.*, the protocol, the corresponding documents, the research team) that was approved or had a determination of exempt status are implemented until all applicable approvals are obtained, including approval from the IRB. The only exception to this provision is that modifications may be implemented without IRB approval when necessary to eliminate an apparent and immediate hazard to the human subjects or others, in which case the PI shall notify the IRB promptly of the modifications made and their rationale.

NOTE: A student who is present solely to observe is not considered to be part of the research team. However, if that student (or any other person) participates in any research activity, including human subject recruitment, human subject interaction or intervention, or data gathering or interpretation, then that student would be part of the research team.

4. Ensuring that the entire membership of the research team maintains currency in human subject research training by having completed such training within the last 3 years.

5. Disclosing to the IRB any management plan implemented by the Conflict of Interest Committee as it relates to any conflict of interest in research held by the PI or other investigator.

6. Promptly reporting to the IRB any instance of (a) serious adverse events, (b) unanticipated problems involving risk to human subjects or others, or (c) noncompliance with policies or IRB requirements (see Sections XIV and XV of this Manual).

7. Timely application for continuing review or modification of a protocol, or timely notification of voluntary closure of a human subject research protocol as applicable.

IV. APPLICATION FOR IRB REVIEW

A. Responsible Person - PI. The PI is responsible for timely submission of an application for IRB review that is complete and contains accurate and understandable information, so that the IRB may conduct an efficient and effective review.

B. Approved Forms. The Executive Vice President for Research has the authority and may approve forms that shall be used to apply for IRB review. Suggestions for modifications to the application forms may be forwarded to the Executive Vice President for Research, via the IRB Chair for comment.

C. Application Submitted to IRB Administrative Office. The initiation of the IRB pre-review process of a human subject research project occurs following submission of an application to the IRB Administrative Office.

1. Timeliness: The deadline for submission of complete applications for IRB review is three weeks prior to the scheduled IRB meeting date on which the PI desires the protocol to be reviewed. Earlier submission (*e.g.* 2-3 months prior) is encouraged. PIs should consider the possibility of IRB deferral during its review, especially for complex protocols.

2. Completeness: The IRB Staff will conduct an administrative pre-review screening to evaluate completeness of the application.

a. A complete application will include all applicable completed forms accompanied with supporting documents (including any management plan implemented by the Conflict of Interest Committee for a conflict of interest disclosed by an investigator). A checklist, the first page of the application, developed by the IRB and approved by the Executive VP for Research may be used to guide this process.
b. An incomplete application will not be forwarded for IRB review. The IRB Staff will contact the PI to discuss items required to complete the application.

3. Qualifications of Research Team: The IRB Staff will also evaluate the submitted materials and determine if:

a. Each member listed on the research team roster is current in human subject research training; and
b. No member listed on the research team is on the federal "Excluded Parties List System (EPLS), which is currently searchable through the following link: https://www.sam.gov/.
c. If the research is FDA regulated, then this screening will also ensure that no member of the research team is listed on the FDA lists of disqualified and restricted clinical investigators, currently linked at: http://www.fda.gov/ICECI/EnforcementActions/ucm321308.htm or listed on the FDA debarment list, currently linked at: http://www.fda.gov/ICECI/EnforcementActions/FDADebarmentList/default.htm.

d. An application that does not pass screening will not be forwarded for IRB review. The IRB Staff will return the application that fails the initial screening and contact the PI to discuss reasons for the return.

4. The IRB Staff will accept and date receipt of an application that has passed initial screening criteria and notify the IRB Chair that the application is ready for review.

V. APPLICATION PROCESSING - INITIAL IRB REVIEW PHASE

A. <u>Action by IRB Chair</u>. Upon notification of a pending application for IRB review, the IRB Chair or designee (Vice Chair) shall review the application and has the authority to take one or more of the following steps, as applicable, in order to promote effective and efficient IRB review:

1. Return or hold an application that is incomplete (*e.g.* has missing elements that may not have been noticed during the IRB staff pre-review).

2. Refer a matter to another committee or board in order to seek written advice and other information on a particular issue of expertise (*e.g.* Conflict of Interest Committee, Bio-Safety Committee, Radiation Safety Committee).

3. Make an IRB determination that the research is "not human subject research", using the criteria described in this Manual (*e.g.* Sections III and X).

4. Make an IRB determination that the research is "not conducted under the auspices of the University" using the criteria described in Sections I and II of this Manual.

5. Refer the application for "Collaborative Status" IRB review, consistent with Section IX of this Manual.

6. Refer the application for "Exempt Status" IRB review, consistent with Section VIII of this Manual.

7. Assign the application, along with the scientific validity assessment report, for either:

   a. "Full Board" IRB review (consistent with Section VI of this Manual) or
   b. "Expedited Status" IRB review (consistent with Section VII of this Manual).

VI. FULL BOARD IRB REVIEW PROCESS

A. Introduction. "Full Board" IRB review means a determination is made at a convened meeting of the IRB using the processes described in paragraph II.G and in this Section VI of this Manual.

B. Primary Reviewer. The IRB Chair will directly designate or set the policy for designation of a Primary Reviewer from the IRB membership. The purpose and function of the Primary Reviewer process is to conduct a comprehensive and detailed assessment sufficient to brief the IRB during the meeting and provide recommendations relating to all aspects of the IRB review.

1. Normally, the Primary Reviewer will be a faculty member in the same or similar academic discipline to the type of research project in order to provide the necessary expertise to conduct an efficient and effective primary review.

2. When considered appropriate by the IRB Chair, consultation from an expert outside of the IRB membership may be obtained to promote an efficient and effective primary review. Consultants would provide relevant information to the Primary Reviewer, but would not be considered part of the IRB (if the consultant attends the IRB meeting, they would be considered a "guest" as described in paragraph II.G of this Manual). The documentation of key information provided by consultants will be reflected in the minutes of the particular meeting. The consultant must not have a conflicting interest.

NOTE: A consultant will be deemed to have a "conflicting interest" with a particular research project when that person, their spouse, and/or dependent children either has a personal interest that will be affected by the research result or who is associated with the sponsor or a competitor, or is significantly involved in the design, conduct, or reporting of that research.

3. A copy of the complete application, along with all supporting documentation, will be provided to the Primary Reviewer. In addition, forms and checklists will be available from the IRB Staff to assist the Primary Reviewer in conducting an efficient and effective primary review.

NOTE: The PI may (and is encouraged to) obtain copies of the relevant forms and checklists in order to anticipate and clarify material issues that will be reviewed.

4. The Primary Reviewer may, but is not required to, communicate with the PI about any deficiency identified in the review process in order to allow the PI to take corrective action prior to the convened IRB meeting.

NOTE: The Primary Reviewer must be careful to prevent this pre-meeting communication from resulting in the Primary Reviewer becoming significantly involved in the design of the research project (which, if it did, would then result in that Primary Reviewer having a conflict of interest in reviewing that research project). Also, this pre-meeting communication is a courtesy and the failure to communicate deficiencies prior to the meeting shall not prohibit or inhibit any IRB member from raising concerns and/or withholding a vote of approval based on those deficiencies.

5. The IRB Chair may also request that a Secondary Reviewer from the IRB membership also conduct a thorough review of the application and report out to the full board membership at the convened meeting.
NOTE: This may be useful for large or complex protocol applications.

6. Scientific Validity Assessment**.** A scientific validity assessment will be conducted by the primary reviewer, at least, to provide information to the IRB regarding scientific and statistical issues of the particular research project. Any IRB member may contribute to the scientific validity assessment, as long as they have the necessary expertise and do not have a conflict of interest. Expertise outside of the IRB membership may be sought if necessary to provide input on the scientific validity of the application

a. This scientific validity assessment consists of evaluating the research project from a scientific and statistical perspective and answering the following questions:
    i. Are the qualifications of the PI and any other investigator appropriate to fulfill the responsibilities of investigator relating to the design and conduct of the research project?
    ii. Will addressing the hypothesis or scientific question advance scientific knowledge?
    iii. Is the design of the research project scientifically and statistically sound in order to address the hypothesis or scientific question?
    iv. Are the benefits and risks involved accurately articulated in the application?
    v. Is there any other scientific or statistical issue that should be highlighted for the IRB to conduct its review?
b. Concerns about the scientific validity of the proposed project will be included in the IRB review and retained as part of the case file.

C. <u>Timely Distribution of Materials to IRB Membership</u>. The IRB Staff will distribute a copy of the complete application to each member of the IRB approximately two weeks prior to the scheduled IRB meeting in which that research project is scheduled for review. This is typically done electronically. At the discretion of the IRB Chair, copies of other supporting documents may also be distributed (*e.g.* when a management plan by the Conflict of Interest Committee has been implemented, then that document would normally be distributed to all IRB members). Any IRB member shall have access to all supporting documents, which may be obtained from the IRB staff.

D. <u>Required Criteria for IRB Determination of "Approved"</u>. A determination by the IRB of "Approved" regarding a human subject research project may be made only when the IRB determines <u>all</u> of the following:

1. The risks to human subjects are minimized: (a) By using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and (b) and whenever appropriate, by using procedures already being performed on the human subjects for diagnostic or treatment purposes. This step would include a formal assessment by the IRB whether the research is minimal risk or more than minimal risk.

*NOTE: The term "**risk**" means the probability and magnitude of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study (as distinguished from, for example, the risk of therapies the human subjects would receive even if not participating in the research):*

- *Physical harm includes exposure to minor pain, discomfort, or injury from invasive medical procedures, or harm from possible side effects of drugs.*
- *Psychological harm includes undesired changes in thought processes and emotion (e.g., episodes of depression, confusion, or hallucination resulting from drugs, feelings of stress, guilt, and loss of self-esteem).*
- *Social and economic harm includes embarrassment within one's business or social group, loss of employment, or criminal prosecution. Areas of particular sensitivity are information regarding alcohol or drug abuse, mental illness, illegal activities, and sexual behavior.*

The IRB should not consider possible long-range public policy effects of applying knowledge gained in the research as a risk within its purview.

*NOTE: **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.*

*NOTE: For **people who are incarcerated, 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.*

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

*NOTE: The term "**benefit**" means the potential for a valued or desired outcome or an advantage. The benefits of research fall into two major categories: (1) benefits to human subjects and (2) benefits to society. A potential benefit to the human subject would be the possible advantageous outcomes that might result from participation, such as gaining a better understanding of a disorder or potentially gaining access to an experimental item or procedure that is not available outside of the research context. Care must be exercised to avoid exaggerating the potentiality of benefits to human subjects and or creating the false belief that the specific purpose of the encounter is to administer an individualized treatment plan to benefit (i.e. therapeutic misconception). Society benefits from the research through increased generalized knowledge and the advances made in health, science, safety, and technology based on that knowledge.*

The following are not to be considered a "benefit" of research: any remuneration to a human subject in exchange for volunteering or the personal positive feeling of the human subject from providing a humanitarian or altruistic contribution to another or to society in general. In addition, 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.

NOTE: Evaluation of the risk/benefit ratio is a major ethical judgment that often depends upon prevailing community standards and subjective determinations of risk and benefit.

3. The selection of human subjects is equitable and additional safeguards are implemented for any vulnerable population.

NOTE: In making the equitable assessment of the selection process, the IRB should take into account the purposes of the research and the setting in which the research will be conducted. Human subject selection should include children and adults, male and female, and minority and majority populations unless such

inclusion is inappropriate due to scientific or ethical reasons with due consideration given to the health of the human subjects and purpose of the research.

NOTE: The IRB must be particularly cognizant of the special problems of and requirement of additional safeguards to be implemented in research involving vulnerable populations as described in Section XIII of this Manual (e.g. children, people who are incarcerated, pregnant people, human fetuses, and neonates, individuals with impaired decision-making capacity, University students or employees, or economically or educationally disadvantaged persons).

4. Informed consent will be sought from each prospective human subject or their legally authorized representative and the informed consent will be appropriately documented, as these requirements are further described in Section XII of this Manual.

NOTE: Human subjects, to the degree that they are able, ought to be given the opportunity to choose what will or will not happen to them through a consent process. This consent process consists of three elements: information, comprehension, and voluntariness.

The extent and nature of information to be supplied to the prospective human subject ought to be that which a reasonable volunteer would want to know before making a decision whether to participate in the furtherance of knowledge, fully understanding that the research is neither necessary for their well-being nor perhaps fully understood. Because the information is useful only if it is comprehended, the presentation of such information ought to be adapted to the prospective human subject's capacity and competence. Any agreement to participate ought to be voluntary (i.e. free of coercion and undue influence).

5. A Safety Monitor has been appointed by the IRB for each research project involving more than minimal risk and, when appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of the human subjects.

NOTE: For research involving more than minimal risk to the human subjects, the IRB must appoint by name an IRB Safety Monitor to: Receive and review reports submitted by the PI and to conduct other oversight of the progress of the research as described by the IRB (e.g. recruitment, enrollment, data collection, or data storage and analysis). The IRB Safety Monitor must be qualified by education and/or experience to competently review the reports submitted by the PI and to conduct the oversight measures, if applicable. This may require the IRB Safety Monitor in some projects to be a credentialed physician or other healthcare provider. The IRB Safety Monitor must not be part of the research team but may be a member of the IRB.

NOTE: In making the assessment about adequate provisions for monitoring data, the IRB will determine whether the plan to be used to collect and analyze data as the project progresses is sufficient to enable an ongoing determination of the appropriateness of continuing the research as approved, or whether modifications should be made (e.g. new information to be conveyed to human subjects, changes in recruitment process, changes in risk/benefit analysis), or whether the project should be terminated. Monitoring techniques are to be employed as appropriate to protect the safety of human subjects depending upon the specifics of the research project, including the element of risk involved. The techniques employed to monitor the data collected would, as appropriate, include activities of the research team and/or activities of another body.

6. When appropriate, there are adequate provisions to protect the privacy of human subjects and to maintain the confidentiality of data.

NOTE: The Secretary of HHS will, after consultation with the Office of Management and Budget's privacy office and other Federal departments and agencies that have adopted this policy, issue guidance to assist

IRBs in assessing what provisions are adequate to protect the privacy of subjects and to maintain the confidentiality of data.

NOTE: Although the terms "privacy" and "confidentiality" are used interchangeably by many (even by some government agencies and in many laws), the two terms used here address different concepts. ***Privacy*** *relates to one's control over the extent, timing, and circumstances of sharing one's knowledge, capacities, desires, behavior or other aspects about one's self. The IRB plays a more significant role in protecting privacy of human subjects when the recruitment phase involves a degree of deception about what is being observed or gathered and when there is a waiver of informed consent (because in such cases the human subject does not have the opportunity to decline participating based on privacy concerns).* ***Confidentiality*** *relates to safeguarding information once it is obtained, whether it was voluntarily shared by the human subject or obtained by other means. When private information linked to individuals will be recorded as part of the research design, the protocols must provide for adequate precautions to safeguard the confidentiality of that private information. Private information includes any information the human subject would not want to be released to the general public for any reason, including a desire to avoid psychological, social, or economic harm. The IRB should also be aware of the available provision for waiving documentation of consent when a signed consent form would itself constitute a risk to the human subjects. The IRB is not required to review and approve HIPAA Privacy Rule authorizations or otherwise enforce HIPAA Privacy Rule compliance. Further information about the HIPAA Privacy Rule and research is available from the Office of Compliance and the federal government at http://privacyruleandresearch.nih.gov.*

7. The investigators are qualified to conduct the research.

NOTE: The investigator's professional experience, expertise, and conflicting interests, should be considered and compared to the specifics of the research project, to include its complexity, risk to human subjects, and skill sets.

A separate University policy addresses conflict of interest in research. When a conflict of interest in research is disclosed through that policy, IRB approval will be withheld pending completion of the process described in that other policy. Thereafter, the IRB will independently review the sufficiency of the management plan, as part of its responsibility of protecting the rights and welfare of human subjects. Any desire by the IRB to remove or modify elements of a management plan implemented by the Conflict of Interest Committee shall be communicated to and coordinated with the Conflict of Interest Committee. The IRB has authority to determine an investigator has a conflict of interest (and, then, implement a management plan) even though the investigator's interest is below the threshold established in that other policy. In addition, the investigator will be deemed to be <u>not</u> qualified if that investigator is listed on any excluded party, disbarment, or similar lists described in subparagraph IV.C.3 of this Manual.

8. The schedule for renewal of approval is appropriate to the degree of risk and not less than once per year, except as follows:

a. No continuing review is required, unless the IRB determines otherwise, for research approved through expedited review (discussed in Section VII of this Manual)

b. No continuing review is required, unless the IRB determines otherwise, for research that was reviewed through the limited IRB review process (discussed in Section VIII of this Manual).

c. No continuing review is required, unless the IRB determines otherwise, for research previously approved by the full board that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
(A) Data analysis, including analysis of identifiable private information or

identifiable biospecimens, or (B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

9. When applicable, other special findings exist, as explained elsewhere in this Manual or applicable law.

NOTE: Special findings are those required in other locations within this Manual or in the applicable law as a pre-condition to approval (e.g. findings relating to vulnerable populations, informed consent waivers, and medical device risk).

E. IRB Determinations Other Than Approved. If the IRB determines that all of the criteria of paragraph VI.D. of this Manual are *not* fulfilled, then the IRB determination shall be one of the following:

1. Conditionally Approved. A determination of "conditionally approved" may be made only when the IRB determines that all of the criteria of paragraph VI.D of this Manual would be fulfilled upon the PI satisfying a specific list of conditions, and the IRB expressly prohibits the PI from initiating the research project until final approval is granted by the IRB Chair (which may be granted only upon the PI showing in writing to the IRB Chair or designee how that specific list of conditions has been satisfied).

a. The IRB Chair (or designee) has authority to review the PI's proof of satisfaction of the conditions and determine whether the conditions are actually fulfilled. If so, the IRB Chair has authority to provide final approval. In such cases, the schedule for renewal of approval (i.e. continuing review) is calculated from the date of the IRB meeting, not the final approval of the IRB Chair.

b. The conditions may only be those that are capable of being easily determined to exist or not by the IRB Chair without the exercise of analysis, balancing, or similar level of judgment. Examples of appropriate conditions are correcting a specified typographical error, requiring a specified disclosure be made during the recruitment process, or making specified wording changes. Examples of inappropriate conditions (because these changes themselves should receive IRB review) are stating, "make it easier to understand" or "include comments about privacy" or "lessen the risks a bit more."

2. Deferred with comments. A determination of "deferred with comments" may be made when certain deficiencies are beyond that deemed as appropriate "conditions" as described in above paragraph VI.E.1. of this Manual, but the IRB expects the PI is willing and able to address those deficiencies within a reasonably short period of time.

3. Disapproved. In all other situations, the IRB determination shall be "disapproved" and the case file closed.

F. Announcing Determinations.

1. Announcing IRB Determination to PI.

a. In cases of a determination of "approved," the IRB Chair will, on behalf of the IRB, issue a letter to the PI indicating its determination along with any requirements and constraints imposed. This letter will include an expiration date for the approval (which is the date on which the approval will lapse) and for full board reviewed protocols, that expiration date must be no longer than one year from the date of the approval decision was made regardless of when it was communicated. In cases when the approval was the final step after a previous determination of "conditionally approved," the expiration date for full board reviewed protocols and federally funded studies must be no longer than one year from the date that the full board made the "conditionally approved" determination regardless of when the IRB Chair made final approval. In addition, the informed consent document will be dated with the expiration date by the IRB and made an enclosure to the approval letter. Finally, the letter will include a statement that IRB approval does not alleviate the PI from complying with other laws and regulations that are beyond the scope of IRB review.

b. In cases of a determination of "conditionally approved," the IRB Chair will, on behalf of the IRB, issue a letter to the PI with a list of specific conditions that must be satisfied before initiation of the research project and describing the process of obtaining final approval from the IRB Chair (at which time, that final determination of "approved" would be announced the same as described in subparagraph VI.F.1.a of this Manual).

c. In cases of a determination of "deferred with comments" or "disapproved," the IRB Chair will, on behalf of the IRB, issue a letter to the PI indicating its determination, the reasons for its determination, the circumstances in which the PI may seek additional information regarding the determination, and when (if at all) the protocol is scheduled for further review.

2. Announcing IRB Determination to University. The Executive Vice President for Research shall be notified of IRB determinations by means of the IRB Staff forwarding copies of IRB letters sent to PIs, the IRB Staff forwarding copies of IRB meeting minutes, or other timely and reliable method as determined by the Executive Vice President for Research. This notification will normally be within 45 days of the IRB determination.

3. Announcing IRB Determination to Rosalind Franklin University Health Clinics. If the protocol involves human research activities conducted at the Rosalind Franklin University Health Clinics, the IRB staff shall notify the management leadership of the Health Clinics of the approved research by means of copies of IRB letters sent to PIs or other timely and reliable method as agreed to by the IRB staff and the Health Clinics. This notification will normally be within 5 days of the IRB determination.

G. Additional Review by Executive Vice President for Research.

1. The Executive Vice President for Research has the authority to conduct additional review of any human subject research project that has received an IRB determination of

approval. This additional review includes the discretionary authority to disapprove research that is deemed by the Executive Vice President for Research to be inconsistent with any University policy.

2. A human subject research project that has not been approved by the IRB may not be initiated through the approval of any person, office, committee, or board.

VII. EXPEDITED REVIEW PROCESS

A. <u>Eligibility for Expedited Review Process</u>. A human subject research project is eligible to be reviewed and determinations made under the expedited review process:

1. for proposed minor changes to a currently approved research project, or
2. for proposals that fulfill ALL of the following criteria:
   a. the research activities involve *no more than minimal risk* to human subjects (including, the identification of the human subjects and/or their responses would not reasonably place them at risk of criminal or civil liability or be damaging to the human subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal);
   b. the research is *not considered classified research* involving human subjects;
   c. the research activities are included in *at least one* of the following categories:

   (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 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 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; or.
   NOTE: For these human 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
   (b) from other adults and children (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), considering the age, weight, and health of the human subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected.
   NOTE: For these human 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.

   (3) Prospective collection of biological specimens for research purposes by noninvasive means.
   NOTE: Examples include: (a) hair and nail clippings in a non-disfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent

teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) 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.

NOTE: Routinely employed clinical procedures include the following (not an all inclusive list): oral examinations, nasal examinations, auditory examinations, GYN examinations, and digital rectum examinations. Noninvasive, when applied to a diagnostic device or procedure, means one that does not by design or intention: (a) Penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra, or (b) enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum, or the vagina beyond the cervical os (for purposes of this policy, blood sampling that involves simple venipuncture is considered noninvasive [see also category (2) above], and the use of surplus samples of body fluids or tissues that are left over from samples taken for non-investigational purposes is also considered noninvasive).

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 human subject or an invasion of the human subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

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

NOTE: Some research in this category may fulfill the "exempt status" criteria. 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 fulfill the "exempt status" criteria. 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 human subjects; (ii) all human subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of human subjects; or

(b) where no human subjects have been enrolled and no additional risks have been identified; or

(c) where the remaining research activities are limited to data analysis.

(9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption, where categories 2-8 (above) 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.

B. Expedited Review Process - Overview.

1. The IRB Chair will directly designate or set the policy for the designation of two or more members to conduct the IRB review and make determinations on behalf of the IRB using the expedited review process. In the event the IRB Chair is an investigator in the human research project, then the IRB Vice Chair or the IRB Administrator will designate two or more members to conduct the review and make determinations.

2. Scientific Validity Assessment**.** A scientific validity assessment will be conducted by the primary reviewer, at least, to provide information to the IRB regarding scientific and statistical issues of the particular research project. Additional IRB reviewers may contribute to the scientific validity assessment, as long as they have the necessary expertise and do not have a conflict of interest. Expertise outside of the IRB membership may be sought if necessary to provide input on the scientific validity of the application.

a. This scientific validity assessment consists of evaluating the research project from a scientific and statistical perspective and answering the following questions:
    i. Are the qualifications of the PI and any other investigator appropriate to fulfill the responsibilities of investigator relating to the design and conduct of the research project?
    ii. Will addressing the hypothesis or scientific question advance scientific knowledge?
    iii. Is the design of the research project scientifically and statistically sound in order to address the hypothesis or scientific question?
    iv. Are the benefits and risks involved accurately articulated in the application?
    v. Is there any other scientific or statistical issue that should be highlighted for the IRB to conduct its review?
b. Concerns about the scientific validity of the proposed project will be included in the IRB review and retained as part of the case file.

2. An IRB determination of "Approved" through the use of the expedited review process may be made only when:

a. There is an unanimous decision that the criteria for eligibility for expedited review process are satisfied, as described in paragraph VII.A of this Manual; and

b. There is an unanimous decision that all criteria for an IRB determination of approval pursuant to a full IRB review process are satisfied, as described in paragraph VI.D of this Manual.

3. If there is a determination of "Approved", then the decision will be announced as described in paragraph VI.F of this Manual and additional review may be conducted as described in paragraph VI.G of this Manual. Under the new rules no continuing review is required, unless the IRB determines otherwise, for research approved through expedited review. A recommendation of "Conditionally approved" or "Deferred with comments" may be made through the use of expedited review process. In such a scenario, the PI would revise the application in accord with the reviews and the designated reviewers would review the revised application and come to a unanimous decision.

4. If, for whatever reason, the IRB reviewers cannot come to a unanimous decision concerning approval, then the research project shall be referred for full board IRB review as described in Section VI of this Manual.

5. The IRB Chair shall inform the IRB of every approval determination made under expedited review process at the next scheduled IRB meeting.

VIII. EXEMPT STATUS PROCESS

A. <u>Eligibility for Exempt Status Process</u>. A research project is eligible for exempt status when the only involvement of human subjects in research activities will be in one or more of the following categories (46.104(d)(1-8)):

NOTE: The exemptions at this section do not apply to research that involves the vulnerable population of people who are incarcerated, except for research aimed at involving a broader subject population that only incidentally includes people who are incarcerated.

1. Research, conducted in established or commonly accepted educational settings, 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 research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

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

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;

NOTE: For research involving children and involving educational tests or the observation of public behavior, the above Category 2.a criterion may be used only when the investigator(s) do not participate in the activities being observed.

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

NOTE: For research involving children and involving educational tests or the observation of public behavior, the above Category 2.b criterion may be used only when the investigator(s) do not participate in the activities being observed.

c. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by § 46.111(a)(7) [internal note: this is the approval criteria relating to protecting privacy and confidentiality].

NOTE: The above Category 2.c criterion may not be used for research involving children.

3. (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 if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

a. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

b. Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

c. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by § 46.111(a)(7).

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

NOTE: For category 3, 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.

NOTE: Category 3 exemption does not apply to research involving children.

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

a. The identifiable private information or identifiable biospecimens are publicly available;

b. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

c. The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under the HIPAA Privacy Rule, 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

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

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

NOTE: For category 5, 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 other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

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

a. wholesome foods without additives are consumed or,

b. a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or an 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. 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 following determinations:

(a) Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements of Section XII.A, paragraphs 1-4 and 6, and Section XII.D of this Manual;

(b) Broad consent is appropriately documented or waiver of documentation is appropriate, in accordance with XII.J and K of this Manual (addressing documentation of information consent and waiver of documentation of informed consent); and

(c) If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

8. Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

a. Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with the requirements of Section XII.A, paragraphs 1-4 and 6, and Section XII.D of this Manual;

b. Documentation of informed consent or waiver of documentation of consent was obtained in accordance with XII.J and K of this Manual (addressing documentation of information consent and waiver of documentation of informed consent);

c. An IRB conducts a limited IRB review and makes the determination required by Section VI.D.6 (addressing adequate provisions to protect the privacy of subjects and confidentiality of data) of this Manual and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph 8.a of this section; and

d. 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.

(NOTE: FDA-regulated research protocols are not eligible for exempt status)

B. Exempt Status Process - Overview

1. The IRB Chair will designate one or more IRB members to conduct the IRB review and make determinations on behalf of the IRB using exempt status process. In the event the IRB Chair is an investigator in the human research project, then the IRB Vice Chair will appoint one or more persons for this purpose. An IRB determination of "exempt status" may be made only when the criteria for eligibility for exempt status are satisfied.

NOTE: Even though a research project meets the eligibility criteria for exempt status, a decision may be made to refer it for another form of IRB review.

2. If there is a determination of "exempt status," then the IRB Chair will, on behalf of the IRB, issue a letter to the PI indicating its determination along with any requirements and constraints imposed.

a. A determination of "exempt status" does not expire.

b. The PI of an exempt status project must notify the IRB of any change in circumstances that relate to the exempt status determination in a very timely manner.

c. The IRB may request information from the PI to review the activities or site of performance of an exempt status project that is underway in order to ensure continued ethical protections.

d. The PI must file a voluntary closure with the IRB when an exempt status project that has been completed.

3. If, for whatever reason, there is not a determination as described above, then the research project shall be referred for full or expedited IRB review as appropriate and described in Sections VI and VII of this Manual.

4. The IRB Chair shall inform the IRB of every determination made under exempt status process at the next scheduled IRB meeting.

IX. COLLABORATIVE RESEARCH PROJECTS

A. Overview

It is not uncommon for researchers located at different institutions or locations to collaborate on human subject research projects and federal regulations on this topic have changed recently. Examples of collaborative research include:

1. A Rosalind Franklin University (RFU) investigator wishes to participate in a multi-center clinical trial or other type of human subject research project.

2. A RFU investigator wishes to conduct studies at this University as well as at an external, unaffiliated clinic.

3. A RFU investigator wishes to conduct a study at a community-based site with a community partner.

4. A RFU investigator wishes to share identifiable or coded data/images/specimens collected for a study with researchers at another institution for specific analyses.

In all cases of collaborative multisite human subject research, some type of formal "reliance agreement" such as an IRB authorization agreement (IAA), individual investigator agreement (IIA), memoranda of understanding (MOU), collaborative agreement, or cooperative agreement (this term is used by the FDA to refer to multi-center cooperative research projects), will be needed.

B. Federally Funded vs. Non-Federally Funded Projects

Effective January 25, 2018, NIH-funded multi-site studies, where each site will conduct the same protocol involving non-exempt human subjects research, whether supported through grants, cooperative agreements, contracts, or the NIH Intramural Research Program must use a single Institutional Review Board (sIRB). NIH-funded multi-site studies mean that the same protocol involving non-exempt human subjects research is being conducted at more than one site and is wholly or partially funded by NIH. The sIRB review requirement will be extended to other federal agencies in 2020; it is NOT required for studies that are not NIH funded.

Protocols that address the same research questions, involve the same methodologies, and evaluate the same outcomes are considered to be the "same research protocol." Additionally, sites that are accruing research participants for studies that are identical except for variations due to local context consideration would be considered to be conducting the "same research protocol." If a study involves a separate site for study coordination or coordination of data and statistical analyses, and the site is conducting the same protocol as the other participating sites, then all sites would be expected to rely on the designated single IRB.

Collaborative projects where different sites are conducting different parts of the research are not considered to be multi-site research and do not have to use sIRB. The sIRB requirement does not apply to studies that are:

- Conducted at foreign sites.
- Funded through career development (K), institutional training (T), or fellowship awards (F).
- Where sIRB review is prohibited by federal, tribal, or state law, regulation or policy.

Local sites are typically required to provide local context information to the sIRB as well as to establish reliance agreements with the lead site. There are usually costs associated with participation in sIRB projects that PIs need to budget for.

C. Who can Serve as the single IRB (sIRB)

Basically, any IRB with a Federal-wide assurance (FWA) filed with the Office for Human Research Protections (OHRP) can serve as a sIRB including:

- The IRB at the applicant/other (lead) PI's site
- The IRB at a participating site
- The IRB at a non-participating site
- Commercial IRBs
- A NIH IRB *(under specific circumstances).*
- An IRB specifically set up for an already established and funded research network or consortium
- A Trial Innovation Network (TIN) IRB *(There are currently three such Central IRBs at Utah, Hopkins, and Vanderbilt) available free of charge).*

In most situations, the lead PI of the study, in collaboration with the IRB office at the lead PI's institution, will select the sIRB. The selected IRB must be willing to serve as the sIRB, and all of the participating sites must agree to rely on the sIRB.

D. SMART IRB (Streamlined, Multisite, Accelerated Resources for Trials IRB Reliance platform)

The SMART platform (https://smartirb.org/resources/) provides a roadmap for institutions to implement NIH Policy on sIRB use for multisite research. SMART IRB may be used for any study that is eligible for IRB reliance, regardless of funding source.

It is important to note that SMART IRB is not an IRB; rather, it's a platform that offers a master IRB reliance agreement (the SMART IRB Agreement) and a web-based system (SMART IRB's Online Reliance System) which provides a centralized process for participating institutions and their investigators to request, track, and document study-specific reliance arrangements. RFUMS is a participating institution with SMART IRB.

E. IRB Authorization Agreements (IAA)

In multi-site projects that are non-federally funded, an IAA type of reliance agreement that designates one IRB as the "reviewing IRB or IRB of record" that will review and have oversight

of the human subject research conducted at two or more institutions. In order to enter into an IAA, both institutions must have Federal Wide Assurances (FWA) and their IRB and Institutional Officials must vet and agree to the agreement. Investigators and research staff are not authorized to sign an IAA themselves.

F. Individual Investigator Agreements (IIAs)

This type of agreement is appropriate when external (non-RFUMS) personnel will be directly involved as investigators in a study (e.g., administering surveys, obtaining informed consent, reviewing medical records, data analysis) if no other agreements are in place. Basically, IIAs bind independent investigators or investigators at institutions that do not already have agreements with the federal government through a FWA. Requests for IIAs for external personnel are considered by the IRB on a case-by-case.

G. Establishing Reliance Agreements

The review of a collaborative project between more than one research site depends on the types of IRB reliance agreements that have been agreed upon. Because of the complexity of this issue, the investigator should initiate discussions of this issue in advance to allow initial determination of what the IRB will allow and what type of formal reliance agreements will be needed. The IRB and the Institutional Official determines whether the University will serve as the sIRB or the IRB of record for a multisite study or will cede to another IRB is appropriate on a case-by-case basis. Some considerations are as follows:

1. Rosalind Franklin University may agree to serve as the sIRB or "IRB of record" for a multisite study if:

   a. The study is minimal risk and the role of the external site or personnel is either limited or very straightforward (e.g., administration of a single survey, assisting with recruitment of subjects).
   b. The role of the external site or personnel is limited to activities such as data analysis, consultation, or other administrative roles.

2. Rosalind Franklin University will typically not consider serving as the sIRB or "IRB of record" in the following situations/circumstances:

   a. Rosalind Franklin University faculty, staff, or students are not involved in the research.
   b. The external site is the coordinating center for a clinical trial (regardless of phase).
   c. The study is more than minimal risk and the role of the external site or external personnel is substantial (e.g., interaction with subjects, conduct of study procedures).
   d. The Rosalind Franklin University IRB does not have sufficient knowledge of the local context to assume oversight for sites or personnel that will ensure protection of human subjects. This may include sites or personnel located in other states or international locations;

3. Rosalind Franklin University may cede to (authorize) another sIRB for review and oversight for a multisite study in the following situations/circumstances:

   a. The project is federally funded and SMART IRB is used for reliance agreements or,
   b. The study is not federally funded but involves an existing IRB reliance/assurance partner, is minimal risk, and the role of the Rosalind Franklin University personnel is limited and straightforward.

4. Rosalind Franklin University will typically not cede to another institution's IRB to review and provide oversight in situations including, but not limited to, the following situations/circumstances:

   a. The study not federally funded, is more than minimal risk, and the role of Rosalind Franklin University personnel is substantial (e.g., interaction with subjects, conduct of study procedures).
   b. The study qualifies as a Veteran's Administration (VA) study (e.g., veterans will be enrolled, the PI conducts the research under a VA appointment, VA facilities will be used).
   c. The proposed IRB of record does not have sufficient knowledge of local context (as required by federal guidelines) to assume IRB oversight.
   d. A study team member has a conflict of interest that requires a management plan and the management plan prohibits or limits activities that the individual can engage in related to human subjects research.

H. Independent Commercial IRBs and Industry-Sponsored Research

Some industry sponsors of human subject research trials require research sites to use an independent (commercial) single IRB (sIRB) as a condition of conducting the trial and are willing to cover the costs associated with that. Other sponsors may encourage use of a designated independent sIRB, and give site selection preferences to sites willing to rely on it. There are a number of reputable commercial IRBs that are currently active. RFUMS has, or would be willing to consider establishing reliance agreements with major commercial IRBs for industry-sponsored studies on an as-needed basis.

External IRBs must be used for some research activities that are subject to FDA regulation. A research activity is subject to FDA regulation if:

1) the activity involves any use of a drug, other than the use of marketed drugs in the course of the practice of medicine; OR
2) the activity involves the evaluation of a device for safety or efficacy; OR
3) data will be submitted to or held for inspection by FDA.

Below are scenarios under which FDA regulated research which require the use of an external IRB:

1) FDA regulated research trials that are funded by an industry (for-profit organization) partner.

2) FDA regulated research that requires FDA approval of an Investigational Device Exemption (IDE) application-link or an Investigational New Drug (IND) application-link.
3) Humanitarian Use Device projects (see Appendix D)
4) Emergency Research and Emergency Use projects (see Appendix E)

X. CODED PRIVATE INFORMATION OR BIOLOGICAL SPECIMENS

A. Introduction. A research project that involves coded private information or biological specimens might, in fact, not fit the definition of human subject research, even when the information or specimens are to be collected in the future (*e.g.* from medical records or from a tissue repository). Nevertheless, consistent with federal government guidance, research involving coded private information or biological specimens will be processed as human subject research, unless a contrary determination is made consistent with this section.

B. Eligibility Criteria. The eligibility criteria needed to establish that a research project involving coded private information or coded biological specimens is not "human subjects research" require fulfillment of all of the following:

1. The private information or biological specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals;

2. The investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or biological specimens pertain because:

   a. the key to decipher the code is destroyed before the research begins; or
   b. the investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased; or
   c. there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
   d. there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

3. The research project is not regulated by the FDA.

C. Review Process.

1. The IRB Chair will designate one or more IRB members to conduct the IRB review and make determinations on behalf of the IRB. An IRB determination that a research project involving coded private information or coded biological specimens fits the definition of "not human subject research" may be made only when:

   a. The research is not regulated by the FDA; and
   b. The eligibility criteria are satisfied, as described above in Section X.B.

2. A determination made through the use of this process that the research is "not human subject research" would be announced as described in paragraph VI.F of this Manual and additional review may be conducted as described in paragraph VI.G of this Manual. This

determination will not expire, so long as there is no change in circumstances that relate to the eligibility criteria. Accordingly:

a. If, for any reason, the investigator knows or may be able to readily ascertain the identity of the individuals to whom the previously obtained private information or specimens pertain, then the research activity would become human subject research causing the approval to expire and the remaining provisions of this Manual become applicable.
b. If, for any reason, the PI desires to change a circumstance that relates to the eligibility criteria, that desire must be communicated through an application to the IRB before such a change is implemented.

3. The IRB Chair shall inform the IRB of any and all determinations made under this section at the next scheduled IRB meeting.

4. If, for whatever reason, the determination was that the research "is human subject research", then the research project would be subject to the remaining provisions of this Manual.

XI. CONTINUING REVIEW AND VOLUNTARY CLOSURE

A. Introduction. For research reviewed by the full board, IRB determinations of "approved" regarding human subject research will expire on a predetermined date, which would have been selected by the IRB based on the degree of risk of the research project and within one year of the date of approval. Continuing review will not apply for the following:

1. No continuing review is required, unless the IRB determines otherwise, for research approved through expedited review.
2. No continuing review is required, unless the IRB determines otherwise, for research that was reviewed through the limited IRB review process (discussed in Section VIII of this Manual).
3. No continuing review is required, unless the IRB determines otherwise, for 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: (A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or (B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

Continuing review provides the IRB the opportunity to determine whether the IRB determination of approved should be continued and is an essential part of protecting the rights and welfare of human subjects. The PI, for all human research projects, including those with a determination of exempt status, must seek voluntary closure when the study is complete, or will be terminated for other reasons, as described in subparagraph C of this Section.

B. Renew IRB Approval. When the PI desires the research project to remain active (including for long-term follow-up of human subjects or for collection or analysis of private identifiable information) beyond the expiration date for IRB approval:

1. The PI must apply for continuing IRB review prior to the expiration of the existing approval.

    a. The failure to apply in a timely manner before expiration of the existing approval will be handled by the IRB as a matter of noncompliance with policies or IRB requirements, in accordance with section XV of this Manual.
    b. The failure to obtain IRB approval prior to the expiration date of the existing IRB approval will result in a lapse in approval. In such a case, the PI must cease recruitment and all other research activities, other than those that are necessary to protect the rights and welfare of the human subjects, during the period of lapse of approval. A violation of the preceding sentence will be handled by the IRB as a matter of noncompliance with policies or IRB requirements, in accordance with section XV of this Manual.

2. Continuing review through seeking a renewal of IRB approval involves the same criteria as the initial review plus a review of any new, relevant information. This new information includes a self-assessment and status report that contains the number of

human subjects accrued, a summary of adverse events, any unanticipated problems involving risks to human subjects or others, any serious or continuing noncompliance with the policies, requirements, or determinations of the IRB, any withdrawal of human subject(s) from the research, any complaints about the research, interim findings of the research project, and recent relevant literature.

C. <u>Voluntary Closure</u>. When the PI does not desire a human research project to remain active (because the study is completed or for other reasons):

1. The PI must apply in a timely manner to voluntarily close the research project such that the application is delivered to the IRB administration office prior to expiration of the existing IRB approval. If the PI fails to apply before the period of approval ends, then such failure is to be handled by the IRB as a matter of noncompliance with policies or IRB requirements, in accordance with section XV of this Manual.

2. The IRB (typically this is done by a member designated by the IRB Chair and reported to the full committee at the next meeting) may approve an application for voluntary closure when it determines that:

a. the cessation of all research activities will not itself create a harm to the welfare or safety of the human subjects, and
b. further IRB oversight is not warranted.

XII. INFORMED CONSENT

A. General Requirements. Unless expressly provided otherwise in this Manual:

1. 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.

2. 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.

3. 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.

4. 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.

5. Except for broad consent:
   a. 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.
   b. 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.

6. 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.

B. Basic Elements of Informed Consent. Except as provided in the provisions in this Manual regarding broad consent or waivers or alternations of informed consent, the following information shall be provided to each subject or the legally authorized representative:

1. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental;

2. A description of any reasonably foreseeable risks or discomforts to the subject;

3. A description of any benefits to the subject or to others that may reasonably be expected from the research;

4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

6. 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;

7. 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;

8. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled; and

9. One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

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

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

C. <u>Additional Elements of Informed Consent</u>. Except as provided in the provisions in this Manual regarding broad consent or waivers or alternations of informed consent, one or more of the following, when appropriate, shall also be provided to each subject or the legally authorized representative:

1. 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;

2. 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;

3. Any additional costs to the subject that may result from participation in the research;

4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

5. 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 subject;

6. The approximate number of subjects involved in the study;

7. 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;

8. A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and

9. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

D. Broad Consent. 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 nonresearch purposes) is permitted as an alternative to the informed consent requirements in paragraphs B and C of this section. 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:

1. The information required in paragraphs B.2, B.3, B.5, and B.8 and, when appropriate, C.7 and 9 of this section;

2. 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;

3. 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;

4. 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);

5. 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;

6. 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

7. 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.

E. <u>Waiver or Alteration of Consent in Certain Public Benefit and Service Program Research</u>.

1. Waiver. An IRB may waive the requirement to obtain informed consent for research under paragraphs A through C of this section, provided the IRB satisfies the requirements of paragraph E.3 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 at paragraph D 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.

2. 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 paragraphs B and C of this section provided the IRB satisfies the requirements of paragraph E.3 of this section. An IRB may not omit or alter any of the requirements described in paragraph A of this section. If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under paragraph D of this section.

3. 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 or procedures; or

(D) Possible changes in methods or levels of payment for benefits or services under those programs; and

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

F. <u>Waiver or Alteration of Elements of Informed Consent</u>. The failure to provide information and solicit consent, for whatever reason, potentially threatens the ethical principle of respect for persons. Information about the risks may not be withheld for the purpose of eliciting the cooperation of human subjects and truthful answers must always be given to direct questions.

1. Waiver. An IRB may waive the requirement to obtain informed consent for research under paragraphs A through C of this section, provided the IRB satisfies the requirements of paragraph F.3 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 at paragraph (d) 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

2. 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 paragraphs B and C of this section provided the IRB satisfies the requirements of paragraph F.3 of this section. An IRB may not omit or alter any of the requirements described in paragraph A of this section. If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under paragraph D of this section.

3. 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 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.

NOTE: Per Illinois law (410 ILCS § 50/3.1), this particular exception to informed consent requirements is inapplicable in some cases where the human subject also has the status of a patient. That Illinois law reads:

> *(a) Any patient who is the subject of a research program or an experimental procedure, as defined under the rules and regulations of the Hospital Licensing Act, shall have, at a minimum, the right to receive an explanation of the nature and possible consequences of such research or experiment before the research or experiment is conducted, and to consent to or reject it.*
> *(b) No physician may conduct any research program or experimental procedure on a patient without the prior informed consent of the patient or, if the patient is unable to consent, the patient's guardian, spouse, parent, or authorized agent.*
> *(c) This Section shall not apply to any research program or medical experimental procedure for patients subject to a life-threatening emergency that is conducted in accordance with Part 50 of Title 21 of, and Part 46 of Title 45 of, the Code of Federal Regulations.*

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

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

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

H. Posting of Clinical Trial Consent Form.

1. For each clinical trial conducted or supported by a Federal department or agency, one IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal Web site that will be established as a repository for such informed consent forms.

2. If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal Web site (e.g. confidential commercial information), such Federal department or agency may permit or require redactions to the information posted.

3. 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.

I. Additional Requirements of Other Laws. These informed consent requirements and waiver criteria of this Manual do not preempt any applicable federal, state, or local laws (including tribal law 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. Legal advice from the General Counsel or other legal counsel representing the University may be sought regarding the applicability of other laws.

J. Documentation. Unless of waiver is granted, the informed consent must be documented as follows:

1. Informed consent shall be documented by the use of a written form approved by the IRB signed and dated by the human subject or the human subject's legally authorized representative. A copy shall be given to the person signing the form.

2. The written form may be either of the following:

a. A written document that embodies the elements of informed consent as required in this Manual. The form may be read to the human subject or the human subject's legally authorized representative; but, in any event, the investigator shall give either the human subject or the representative adequate opportunity to read it before it is signed and dated; or

b. A short form written document that states that the elements of informed consent that are required in the Manual have been presented orally to the human subject or the human subject's legally authorized representative. When this method is used, there must be a witness to the oral presentation. Also, the IRB shall approve a written summary of exactly what is to be said to the human subject or the representative. Only the short form itself is to be signed and dated by the human subject or the representative. However, the witness shall sign and date both the short form and a copy of the summary, and the person actually obtaining consent shall sign and date a copy of the summary. A copy of the summary shall be given to the human subject or the representative, in addition to a copy of the short form.

K. Waiver of Documentation. The IRB may waive the requirement for the investigator to obtain a signed informed consent form for some, or all human subjects if it finds either:

1. That the research is not subject to FDA regulation and the only record linking the human subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. That being the case, each human subject will be asked whether the human subject wants documentation linking the human subject with the research, and the human subject's wishes will govern; or

2. That the research presents no more than minimal risk of harm to human subjects and involves no procedures for which written consent is normally required outside of the research context.

NOTE: When the documentation requirement is waived, the IRB may require the investigator to provide human subjects with a written statement regarding the research. If so, the IRB will review the proposed written statement.

L. Additional Requirements of Other Laws. These requirements regarding documentation of informed consent and waiver criteria of this Manual do not preempt applicable federal, state, or local laws (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe) that impose requirements related to documentation of informed consent. Legal advice from the General Counsel or other legal counsel representing the University may be sought regarding the applicability of other laws.

M. Emergency Treatment. 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).

XIII. VULNERABLE POPULATIONS

A. General Requirement for All Projects. The IRB shall assess the human subject selection criteria, location of recruitment, and other relevant information to determine whether the research involves a vulnerable population. If so, additional affirmative safeguards must be included in the protocol (usually in the recruitment phase but often in other phases as well) to specifically address the basis for vulnerability (i.e. address diminished capacity and/or diminished sense of voluntariness).

1. The IRB Chair, when anticipating an IRB review of a human subject research project involving a vulnerable population, will strive to ensure that at least one person conducting the review is knowledgeable about or has recent experience with that vulnerable population such that the person is able to appreciate the basis of the vulnerability of that population. This may be also accomplished by obtaining information from a consultant who is knowledgeable about or has recent experience with that vulnerable population.

2. The IRB, when considering additional safeguards, will consider observing the recruitment phase when the IRB has continuing concerns whether the other affirmative safeguards would effectively address the basis for vulnerability.

B. Impaired Decision-Making Capacity. Human subject research projects may involve the vulnerable population of individuals with impaired decision-making capacity (see Definitions in Appendix B) only when the IRB determines there are safeguards to address the vulnerabilities associated with the impairment and:

1. That an effective process will be used to determine whether the human subject lacks decisional capacity and that an effective process for reassessments will be made as appropriate to ascertain a change in capacity.

2. Whenever any of the processes described in XIII.B.1 results in a determination of lack of decisional capacity:
   a. an effective process will be used to identify the appropriate legally authorized representative; and
   b. an effective process will be used to solicit the human subject's assent or an ethically justifiable reason why no such assent ought to be sought.

C. University Students. Human subject research projects may involve the vulnerable population of students of Rosalind Franklin University only when the IRB determines both of the following:

1. No investigator will personally participate in or be present during any individual solicitation of a student when that investigator also has authority, as a faculty member, to academically evaluate that student in any manner.

2. Participation in a research project by a student may not be considered in any academic evaluation (including awarding extra credit) of the student unless an alternative method

of earning an equivalent amount of credit without participating in any research project exists that does not involve more time or expense than participation in the research.

D. University Employees. Human subject research projects may involve the vulnerable population of employees of Rosalind Franklin University of Medicine and Science only when the IRB determines the following:

1. No investigator will personally participate in or be present during any individual solicitation of an employee when that investigator is the first-level or higher supervisor of that employee.

2. Participation in a research project by an employee may *not* be considered in any performance evaluation, decision related to promotion/demotion, decision related to an increase/decrease in payroll compensation, or similar employment decision.

E. Pregnant People, Human Fetuses, Neonates, or Fetal Material.

1. Pregnant People and Human Fetuses. Human subject research projects may involve the vulnerable population of pregnant people or fetuses only when the IRB determines the following:

a. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant people, have been conducted and provide data for assessing potential risks to pregnant people 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 must be 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 the risk to the fetus is not greater than minimal, and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, then the woman's consent is obtained in accord with the informed consent provisions;

e. 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 this Manual. 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.

f. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

g. For children who are pregnant, assent and permission are obtained in accord with the provisions of policy addressing children as vulnerable population;

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.

2. For Neonates of Uncertain Viability. Human subject research projects may involve the vulnerable population of neonates of uncertain viability (*i.e.* it has not yet been ascertained whether or not a neonate is viable) only when the IRB determines the following:

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 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. Either:

(1) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or

(2) The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

e. 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 informed consent provisions of this Manual. The consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

3. For Nonviable Neonates. Human subject research projects may involve the vulnerable population of nonviable neonates only when the IRB determines the following:

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 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. Vital functions of the neonate will not be artificially maintained;

e. The research will not terminate the heartbeat or respiration of the neonate;

f. There will be no added risk to the neonate resulting from the research;

g. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and

h. The legally effective informed consent of both parents of the neonate is obtained in accord with University informed consent provisions of this Manual, except that the waiver and alteration provisions of informed consent 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 these requirements. 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 these requirements.

4. For Viable Neonates. Human subject research projects may involve the vulnerable population of neonates, after delivery, that have been determined to be viable, only to the extent permitted by and in accordance with the provision in the Manual regarding children as a vulnerable population.

5. For The Placenta, Dead Fetus, or Fetal Material after Delivery: 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. If information is recorded in a manner that living individuals can be identified (either directly or indirectly through identifiers linked to those individuals), then those living individuals are considered human subjects and all relevant provisions of this Manual are applicable.

F. People who are incarcerated. Human subject research projects may involve the vulnerable population of people who are incarcerated only when all of the following provisions are fulfilled:

1. IRB Composition. Human subject research projects may involve the vulnerable population of people who are incarcerated only when:

a. A majority of the IRB conducting the review and making the determination (exclusive of prisoner members) has no association with the prison(s) involved, apart from their membership on the IRB.

b. At least one member of the IRB conducting the review and making the determination shall be a prisoner or a prisoner representative with appropriate background and experience to serve in that capacity; except, when a particular research project is reviewed by more than one IRB, then only one IRB need satisfy this requirement.

2. Permissible Categories of Research. The categories of permissible research are limited to:

a. Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the human subjects;

NOTE: For research involving people who are incarcerated, 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.

b. Study of prisons as institutional structures or of people who are incarcerated as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the human subjects;

c. Research on conditions particularly affecting people who are incarcerated 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 Department of Health and Human Services has consulted with appropriate experts including experts in penology medicine and ethics, and published notice, in the Federal Register, of intent to approve such research; or

d. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well being of the human subject. In cases in which those studies require the assignment of people who are incarcerated 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 Department of Health and Human Services has consulted with appropriate experts, including experts in penology medicine and ethics, and published notice, in the Federal Register, of intent to approve such research.

3. IRB Determinations. Human subject research projects may involve the vulnerable population of people who are incarcerated only when the IRB determines the following:

a. The research under review represents one of the categories of research permissible as defined in subparagraph XIIIF2 (above);

b. 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;

c. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;

d. Procedures for the selection of human subjects within the prison are fair to all other people who are incarcerated and immune from arbitrary intervention by prison authorities or people who are incarcerated. Unless the PI provides to the IRB justification in writing for following some other procedures, control human subjects must be selected randomly from the group of available people who are incarcerated who meet the characteristics needed for that particular research project;

e. The information is presented in language that is understandable to the prisoner population;

f. 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

g. Where the IRB finds there may be a need for follow-up examination or care of human subjects after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual people who are incarcerated' sentences, and for informing human subjects of this fact.

4. Office of Human Research Protections (OHRP) Determination. Human subject research projects that are supported by HHS may involve the vulnerable population of people who are incarcerated only after the University seeks and obtains, through written correspondence, from OHRP authorization to conduct the research. The request letter to OHRP must include:

a. a certification of compliance with 45 C.F.R. § 46.305;
b. the name and address of the University;
c. identification of the research protocol and any HHS grant application.

G. Children.

1. Minimal Risk to Children Projects. Human subject research projects that the IRB has determined involve only minimal risk to children may involve the vulnerable population of children only if the IRB determines that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as described in subparagraphs XIII.G.4 & 5 of this Manual.

2. More Than Minimal Risk to Children Projects.

a. Prospect of Direct Benefit. Human subject research projects that the IRB has determined involve more than minimal risk to children, but that risk is presented by an intervention or procedure that holds out the prospect of direct benefit to the participating child or by a monitoring procedure that is likely to contribute to the child's well-being, may involve the vulnerable population of children only if the IRB determines:

(1) The risk is justified by the anticipated benefit to the participating children;
(2) The relation of the anticipated benefit to the risk is at least as favorable to the participating children as that presented by available alternative approaches; and
(3) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as described in subparagraphs XIII.G.4 & 5 of this Manual.

b. No Prospect of Direct Benefit. Human subject research projects that the IRB has determined involve more than minimal risk to children and that risk is presented by an intervention or procedure that does not hold out the prospect of direct benefit to the participating child or by a monitoring procedure that is not likely to contribute to the child's well-being may involve the vulnerable population of children only if the IRB determines:

(1) The risk represents only a minor increase over minimal risk;
(2) The intervention or procedure presents experiences to the participating children that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
(3) The intervention or procedure is likely to yield generalizable knowledge about the participating children's disorder or condition which is of vital importance for the understanding or amelioration of their disorder or condition; and

(4) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as described in subparagraphs XIII.G.4 & 5 of this Manual.

3. Assent. Generally, the IRB may not approve a human research project that involves the vulnerable population of children unless it determines there are adequate provisions for soliciting assent from the children (*i.e.* an affirmative agreement to participate in the research; mere failure to object is not, by itself, assent) and documenting that assent. This determination may be as it relates to all children to be involved in the research project or for each child. The only exceptions are:

a. Child(ren) is (are) Not Capable. If, after taking into account the ages, maturity, and psychological state of the children involved, the IRB determines that the capability of the child(ren) is(are) so limited that the child(ren) cannot reasonably be consulted.

b. Waiver Criteria Fulfilled. To the extent adequate provisions are not made, the IRB determines that the criteria identical to the waiver of informed consent and/or waiver of documentation of informed consent contained in this Manual are fulfilled.

c. Prospect of Direct Benefit. The IRB determines that 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.

4. Permission. Generally, the IRB may not approve a human research project that involves the vulnerable population of children unless it determines there are adequate provisions for soliciting and documenting the permission of each child's parents or guardian by using the criteria applicable to soliciting and documenting informed consent (including waiver provisions) as contained in this Manual.

a. The permission of the child's parents means the permission of both parents of the child unless (*i.e.* permission of one parent is sufficient) when:

(1) The IRB determines that there is only minimal risk to children.

(2) The IRB determines that there is more than minimal risk to children but the risk is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual participating child, or by establishing a monitoring procedure that is likely to contribute to the participating child's well being.

(3) 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.

b. In addition to the general provisions for waiver of informed consent contained in this Manual, if the IRB determines that a research project is designed for conditions or for a population of children for which parental or guardian permission is not a reasonable requirement to protect the participating children (*e.g.* neglected or abused children), the IRB may waive the parental permission requirements, provided an

appropriate mechanism for protecting the children who will participate as human 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 human subjects, and their age, maturity, status, and condition.

5. Wards of the State. Children who are wards of the state or any other agency, institution, or entity can be included in research where 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 human subject, or by a monitoring procedure which is not likely to contribute to the well-being of the human subject *only if*:

a. The research is either:

(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 human subjects are not wards.

b. The IRB requires 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.

XIV. UNANTICIPATED PROBLEMS AND SERIOUS ADVERSE EVENTS

A. <u>Prompt Reporting by PI</u>. Without delay and no later than 7 days, the PI must make a written report to the IRB Chair or their designee (*e.g.* Safety Monitor) of each situation that is either:

1. A serious adverse event, or
2. An unanticipated problem involving risk to human subjects or others.

*NOTE: An "**adverse event**" is any undesirable effect upon a human subject occurring during or within a reasonable time after the conduct of research activities (i.e. the process of intervention or interaction with a human subject and/or the process of collection of identifiable private information about a human subject). An adverse event is "**serious**" when the undesirable effect is:*

a. a physical harm or injury characterized as death, life-threatening condition, in-patient hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect, requires medical or surgical intervention to prevent any of the aforementioned physical harms; or
b. a psychological, social, or economic harm or injury of similar magnitude.

*NOTE: The phrase "**unanticipated problem involving risk to human subjects or others**" means any incident, experience, or outcome that meets all of the following criteria:*

a. unexpected in terms of its nature, its severity, or its frequency (required considerations are what was disclosed during the recruitment process and what was described in the protocol-related documents);
b. related or having a reasonable possibility of being related to the participation in the research (required considerations include whether the sole cause can be identified and what is the natural progression of any pre-existing disease, disorder, or condition); and
c, suggests a greater risk of harm for human subjects or others (in terms of its probability or magnitude of physical, psychological, economic, or social harm.

NOTE: This report will use a form developed by the IRB and will include (1) identification of the research project and PI; (2) a detailed description of the event, incident, experience, or outcome that addresses elements in the relevant definitions; and (3) a description of any modifications to the research project that have been taken or are proposed in order to protect the rights and welfare of the human subjects or others.

<u>B. IRB Review of Report.</u>

1. The IRB Chair or designee will take steps to gather relevant information as deemed appropriate to brief and enable review by the IRB at its next meeting.

2. The IRB, at its next convened meeting, will review the report and other relevant information gathered and will:

a. determine whether that situation meets the definition of an "unanticipated problem involving risk to human subjects or others" using the definition in the note under subparagraph XIV.A.2

b. determine whether it is appropriate to "suspend" or "terminate" IRB approval and, if so, take such action.

*NOTE: "**Suspension of approval**" means an action taken by the IRB during a convened meeting, within the time period in which there is an existing IRB approval in effect, and that fulfills all of the following criteria:*

- *is based on a determination that involves either (a) serious or continuing noncompliance with policies or IRB requirements; or (b) unanticipated problem involving risk to human subjects or others;*

- *implements a cessation of approval to conduct research activities other than that necessary to protect the rights and welfare of the human subjects as defined by the IRB; and*
- *contemplates a potential for approval to be granted upon the occurrence of some event or passage of time as expressed in the IRB determination letter.*

*NOTE: "**Termination of approval**" means an action meeting the criteria of "suspension of approval" except that the action does not contemplate approval will be granted in the future (i.e. cessation of approval is permanent).*

c. review and make determinations in response to any request made by the PI or action taken by the PI, in accordance with this Manual.

NOTE: A situation that amounts to an unanticipated problem to human subjects or others may warrant a desire to modify the research. Examples of modifications could relate to changing inclusion or exclusion criteria; changing monitoring procedures; suspending research or enrollment; changing informed consent disclosures and documentation; providing additional information to enrolled human subjects; shortening the term of IRB approval; and/or referral to other University offices, committees, or boards.

C. Notify Executive Vice President for Research. The IRB Chair will notify the Executive Vice President for Research of each IRB determination made as described in paragraph XIV.B of this Manual. This notification must be promptly and no later than 7 days after the IRB determination was made.

D. Action of the Executive Vice President for Research. The Executive Vice President for Research will take steps to ensure that proper notification to the applicable government agency occurs for each determination of unanticipated problems involving risk to human research subjects or others. These steps will include ensuring that a notification letter is created, determining the relevant government agency or agencies, and providing final approval of the notification letter that is sent. This action will be accomplished within 7 days of receiving notification from the IRB Chair of the occurrence of the unanticipated problem involving risk to human subjects. The contents of such notification letter to the government agency will comply with requirements established by that agency, which normally includes:

1. Name of the University (as the entity conducting the research,
2. Title of the research project and/or grant proposal
3. Name of the PI
4. Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or collaborative agreement);
5. A detailed description of the problem; and
6. Actions the University is taking or plans to take to address the problem (for example, changing inclusion or exclusion criteria; changing monitoring procedures; suspending research or enrollment; changing informed consent disclosures and documentation; providing additional information to enrolled human subjects; shortening the term of IRB approval; suspending or terminating IRB approval; and/or referral to other University offices, committees, or boards).

NOTE: "Relevant government agency" means OHRP for research covered by DHHS regulations; other federal agencies (e.g. DoD or VA) when the research is overseen by those agencies and they require reporting separate from reports to OHRP, and FDA for research that is FDA regulated.

XV. NONCOMPLIANCE WITH POLICIES OR IRB REQUIREMENTS

A. Reporting Concerns and Non-Retaliation. Any person seeking guidance or who becomes aware of any potential, known, or suspected violation of this Manual shall report such matter to the Institutional Review Board (IRB) or, if the concern relates to the IRB, then to the Executive Vice President for Research, so that proper action may be taken. As an alternative, reports may be made to the Office of Compliance directly or through EthicsPoint, Inc. (which allows anonymity), either via its toll-free number (800-254-0460) or its URL (http://rosalindfranklin.ethicspoint.com). No person will be subjected to retaliation, retribution, or reprisal for making a good faith report of, seeking guidance regarding, or participating in the investigation or resolution of a potential, known, or suspected violation of this policy.

B. PI Report to IRB Chair. Without delay and no later than 7 days from its discovery, the PI must make a written report to the IRB Chair or their designee of each act or omission that amounts to a noncompliance with this Manual or IRB requirements.

> *NOTE: This report will use a form developed by the IRB and will include (1) identification of the research project and PI; (2) a detailed description of the noncompliant act or omission; (3) a description of any corrective action taken or proposed; and (4) a description of any modifications to the research project that have been taken or are proposed in order to protect the rights and welfare of the human subjects or others.*

C. Gather Information. Within 7 days of receiving a report of noncompliance with this Manual or IRB requirements:

1. The IRB Chair shall appoint him/herself or another IRB member to gather information, as appropriate, that relates to whether or not there was an act or omission that amounted to noncompliance with this Manual or IRB requirements.

2. In cases where the IRB Chair suspects it may be serious or continuing noncompliance, the IRB Chair must make notification to the Executive Vice President for Research.

*NOTE: **Continuing noncompliance** with this Manual or IRB requirements means a situation involving all of the following criteria, in sequence:*

- *an act or omission that violates any provision of this Manual or IRB requirement;*
- *written notice of the noncompliance provided by the IRB to the PI;*
- *the passage of a reasonable time period to allow corrective action or avoidance of further noncompliance; and*
- *a subsequent and substantially similar act of noncompliance.*

*NOTE: **Serious noncompliance** with this Manual or IRB requirements means an act or omission that is a willful violation and that involves any of the following:*

- *knowingly providing false information to the IRB;*
- *the development of a clear increased risk of a serious adverse event (see subparagraph XIV.A.1 of this Manual); or*
- *is similar in nature or consequence to 1 or 2 above and is so determined by the IRB to be serious.*

D. IRB Review.

1. The IRB Chair will notify the IRB during each IRB meeting of the status of the case until completion.

2. Once the appropriate and relevant information has been gathered, the IRB Chair will brief and provide relevant information to the IRB at a convened meeting. The IRB will review the report and other relevant information gathered and will:

a. determine whether that situation meets the definition of either "serious" or "continuing" noncompliance with policies or IRB requirements using the definitions in the notes under subparagraph XV.C.2 of this Manual.

b. determine whether it is appropriate to "suspend" or "terminate" IRB approval and, if so, take such action.

*NOTE: "**Suspension of approval**" means an action taken by the IRB during a meeting, within the time period in which there is an existing IRB approval in effect, and that fulfills all of the following criteria:*

1. is based on a determination that involves either (a) serious or continuing noncompliance with policies or IRB requirements; or (b) unanticipated problem involving risk to human subjects or others;

2. implements a cessation of approval to conduct research activities other than that necessary to protect the rights and welfare of the human subjects as defined by the IRB; and

3. contemplates a potential for approval to be granted upon the occurrence of some event or passage of time as expressed in the IRB determination letter.

*NOTE: "**Termination of approval**" means an action meeting the criteria of "suspension of approval" except that the action does not contemplate approval will be granted in the future (i.e. cessation of approval is permanent).*

c. review and make determinations in response to any request made by the PI or action taken by the PI, in accordance with this Manual.

NOTE: A situation that amounts to a serious or continuing noncompliance with policies or IRB requirements may warrant modifications to the research. Examples of modifications could relate to changing the PI and members of research team, changing the inclusion or exclusion criteria; changing monitoring procedures; suspending research or enrollment; changing informed consent disclosures and documentation; providing additional information to enrolled participants; shortening the term of IRB approval; suspending or terminating IRB approval; and/or referral to other University offices, committees, or boards.

E. Notify Executive Vice President for Research. The IRB Chair will notify the Executive Vice President for Research of each IRB determination made as described in subparagraph XV.D.2 of this Manual. This notification must be promptly and no later than 7 days after the IRB determination was made.

F. Action of the Executive Vice President for Research. The Executive Vice President for Research will take steps to ensure proper notification to the applicable government agency occurs for each determination of serious or continuing noncompliance with policies or IRB requirements. These steps will include ensuring a notification letter is created, determining the relevant government agency or agencies, and providing final approval of that notification letter to be sent. This action will be accomplished within 7 days of receiving notification from the IRB Chair of the occurrence of the noncompliance. The contents of such notification letter to the government agency will comply with requirements established by that agency, which normally includes:

1. Name of the University (as the entity conducting the research)

2. Title of the research project and/or grant proposal

3. Name of the PI

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

5. A detailed description of the noncompliance; and

6. Actions the University is taking or plans to take to address the problem (for example, changing the PI and members of research team, changing the inclusion or exclusion criteria; changing monitoring procedures; suspending research or enrollment; changing informed consent disclosures and documentation; providing additional information to enrolled participants; shortening the term of IRB approval; suspending or terminating IRB approval; and/or referral to other University offices, committees, or boards.).

NOTE: "Relevant government agency" means OHRP for research covered by DHHS regulations; other federal agencies (e.g. DoD or VA) when the research is overseen by those agencies and they require reporting separate from reports to OHRP, and FDA for research that is FDA regulated.

APPENDIX A

GENERAL POLICY ON OVERSIGHT OF HUMAN SUBJECT RESEARCH AT ROSALIND FRANKLIN UNIVERSITY

Policy Title: Human Subject Research Protection Program

Category: Research
Policy Number: 100
Sponsor: Executive Vice President for Research
Effective Date: April 2, 2003

ROSALIND FRANKLIN UNIVERSITY of MEDICINE AND SCIENCE

INTRODUCTION AND PURPOSE. This policy document articulates the overall policies relating to the conduct and oversight of human subject research conducted under the auspices of the University.

CANCELLATION. All prior policies categorized as "Human Research Protection" are cancelled.

SCOPE AND APPLICABILITY. This policy applies to all University employees and agents, as defined in this policy (which includes all faculty, staff, students, contractors, and volunteers).

POLICY STATEMENTS.

General Policy. All activities relating to the conduct and oversight of human subject research conducted under the auspices of the University shall be in compliance with applicable laws and ethical principles, the Federal Wide Assurance (FWA), and relevant University policies and procedures, and shall be conducted in a manner that protects the rights and welfare of the human subjects involved in that research. Violations of this policy are prohibited and could result in sanctions, including termination.

Responsible Official. The Executive Vice President for Research is the University official with the authority and responsibility to develop, implement, and oversee relevant policies, procedures, and practices in order to ensure compliance with and promote the General Policy stated above. The Executive Vice President for Research has the authority and responsibility to restrict or prohibit particular research activities or categories of research activities in order to ensure compliance with and promote the General Policy stated above.

Cooperation and Coordination. All individuals, committees, and boards involved in activities related to the conduct or oversight of human subject research shall cooperate and coordinate activities in a manner that promotes the General Policy stated above.

Reporting Concerns and Non-Retaliation. Any person seeking guidance or who becomes aware of any potential, known, or suspected violation of the General Policy stated above shall contact the Principal Investigator of the relevant research project, the Institutional Review Board, or the Executive Vice President for Research to ensure proper action is taken. As an alternative,

reports may be made to the Office of Compliance directly or through its toll-free number, which allows anonymity (800-254-0460). No person will be subjected to retaliation, retribution, or reprisal for making a good faith report of, seeking guidance regarding, or participating in the investigation or resolution of a potential, known, or suspected violation of the General Policy stated above.

DEFINITIONS.

Applicable laws and ethical principles. The *applicable laws* include what is known as The Common Rule (codified at various locations, including 45 C.F.R. Part 46) and the FDA regulations (codified at 21 C.F.R. Parts 50 and 56). In addition, several state laws may be applicable, depending upon the specifics of the research project. The *applicable ethical principles* include those set forth in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. In addition, international organizations have developed ethical guidance documents, which may at times be applicable.

Research conducted under the auspices of the University. *Research conducted under the auspices of the University* means research in which a University employee or agent, for the purposes of the research project, obtains: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research.

University employee or agent. *University employee or agent* means any individual who: (1) acts on behalf of the University; (2) exercises University authority or responsibility; or (3) performs University designated activities. "Employee or agent" can include faculty, staff, students, contractors, and volunteers, and others, regardless of whether the individual is receiving compensation from the University.

POINTS OF CONTACT.

Executive Vice President for Research	(847) 578-3251
Institutional Review Board	(847) 578-8713
Office of Compliance	(847) 578-8308

APPENDIX B: DEFINITIONS

Assent. An affirmative agreement to participate in research expressed by someone who lacks the capacity or competence to provide consent. Mere failure to object should not be construed as assent.

Benefit. The potential for a valued or desired outcome or an advantage. The benefits of research fall into two major categories: (1) benefits to human subjects and (2) benefits to society. A potential benefit to the human subject would be the possible advantageous outcomes that might result from participation, such as gaining a better understanding of a disorder or potentially gaining access to an experimental item or procedure that is not available outside of the research context. Care must be exercised to avoid exaggerating the potentiality of benefits to human subjects and or creating the false belief that the specific purpose of the encounter is to administer an individualized treatment plan to benefit (*i.e.* therapeutic misconception). Society benefits from the research through increased generalized knowledge and the advances made in health, science, safety, and technology based on that knowledge.

The following are not considered a "benefit" of research: remuneration to human subjects to volunteer or the personal feeling of humanitarian contribution by the human subject.

Children. The term children (or child) means 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. Applying that definition to research conducted in Illinois, the legal age for consent is 18 except when:

1. the person is married, a parent, or a pregnant person and the research treatments or procedures consist of medical or surgical procedures by a licensed professional (410 ILCS 210/1).

2. the person is a victim of criminal sexual assault or criminal sexual abuse and the research treatment or procedures consist of medical care or counseling related to the diagnosis or treatment by a licensed professional of any disease or injury arising from that criminal offense (410 ILCS 210/3(b)).

3. the person has attained at least 12 years of age and came in contact with a sexually transmitted disease, is an addict or alcoholic, or has a family member who abuses alcohol or drugs and the research treatment or procedures consist of medical care or counseling related to the diagnosis or treatment of that disease (410 ILCS 210/4).

4. the person has attained at least 12 years of age and the research treatment or procedures consist of mental health counseling services or psychotherapy on an outpatient basis when there is not more than 5 sessions and no session will last more than 45 minutes (405 ILCS 5/3-501(a)).

5. The person has attained at least 16 years of age; is a "voluntary recipient" admitted into a mental health facility; the person's parent, guardian, or person *in loco parentis* has

been informed of the admission into the facility; and the research treatment or procedures consist of treatment of the mental illness (405 ILCS 5/3-502).

6. The person has been emancipated by a court order to have legal competency to give consent for the treatments or procedures involved in the research.

NOTE: Legal advice from the General Counsel or other legal counsel representing the University should be sought regarding the application of this definition to research conducted in other jurisdictions and/or for further clarifications of the above.

Clinical Trial. 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.

Conducted under the auspices of the University. The phrase "conducted under the auspices of the University" as it relates to research means research in which a *University employee or agent,* for the purposes of the research project, obtains: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research. The term "**engaged in the research**" in reference to the University or a University employee or agent is also used to denote research that is conducted under the auspices of the University.

NOTE: "University employee or agent" means any individual who: (1) acts on behalf of the University; (2) exercises University authority or responsibility; or (3) performs University designated activities. "Employee or agent" can include faculty, staff, students, contractors, and volunteers, and others, regardless of whether the individual is receiving compensation from the University.

Conflict of Interest. A person who is tasked with reviewing a research project as an IRB member, as part of the scientific validity assessment, as a primary or secondary reviewer, as a designated reviewer, as a consultant, or in any similar role will be deemed to have a "conflicting interest" with a particular research project when that person, their spouse, and/or dependent children either:

1. has a personal interest that:
    a. will be affected by the research result;
    b. is with or associated with the sponsor; or
    c. is with or associated with a competitor of the sponsor;
        -OR-
2. is significantly involved in the design, conduct, or reporting of the research.

Dead Fetus. An expelled or delivered fetus that exhibits no heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, or pulsation of the umbilical cord (if still attached). Note that some organs, tissues, and cells (referred to collectively as fetal tissue) may remain alive for varying periods of time after the total organism is dead.

Decisional capacity. An assessment that a particular person is able to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make and communicate a choice. A person who is legally determined to be incompetent is deemed to lack decisional capacity and that determination may only be altered by law or the court.

Fetal Material. The placenta, amniotic fluid, fetal membranes, and the umbilical cord.

Guardian. An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care. For research conducted in Illinois, the term means a court-appointed guardian of the person, to the extent the court appointment authorizes the guardian to give consent to the treatment or procedures involved in the research and the guardian complies with the court appointment.

> *NOTE: Legal advice from the General Counsel or other legal counsel representing the University should be sought regarding the application of this definition to research conducted in other jurisdictions and/or for further clarifications of the above.*

Human fetus. Human fetus means the product of conception from implantation until delivery.

Human Subject. The terms "human subject" as it relates to research means a living individual about whom an investigator (whether professional or student) conducting research: (i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

Intervention includes 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.

Interaction includes communication or interpersonal contact between investigator and subject.

Private information includes 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).

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

An identifiable biospecimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

> *NOTE: For research subject to FDA regulation, the definition differs. The FDA definition is: an individual who is or becomes a human subject in research, either as a recipient of the test article or as a control; or an individual on whose specimen a medical device is used. A human subject may be either a healthy individual or a patient.*

Impaired Decision-Making Capacity. One whose cognitive or emotional functions are impaired to the extent that capacity for judgment and reasoning is significantly diminished. The basis or reason for this impairment may be due to a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorders), an organic impairment (e.g., dementia), a developmental disorder (e.g., Down's syndrome), the influence of or dependence on drugs or alcohol, a degenerative disease affecting the brain, or a terminally ill status. A person could have impaired decision-making capacity yet have decisional capacity.

Incompetent. A legal determination that one lacks decisional capacity. This legal determination is reflected either in a law for categories of persons *(e.g. generally, children are incompetent)* or a court judgment for a particular individual.

Institution. A residential facility that provides food, shelter, and professional services *(including treatment, skilled nursing, intermediate or long-term care, and custodial or residential care)*. Examples include general, mental, or chronic disease hospitals; inpatient community mental health centers; halfway houses and nursing homes; alcohol and drug addiction treatment centers; homes for the aged or dependent, residential schools for the mentally or physically handicapped; and homes for dependent and neglected children.

Legally authorized representative. A "legally authorized representative" means an an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. 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 nonresearch context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

Applying that definition to research conducted in Illinois, a parent is a legally authorized representative for that person's minor child. Other applications of that definition to research conducted in Illinois are that a legally authorized representative includes the following:

1. a court-appointed guardian of the person, to the extent the court appointment authorizes the guardian to give consent to the treatment or procedures involved in the research and the guardian complies with the court appointment.

2. an "agent" identified in a written Power of Attorney for Health Care document created pursuant to the Illinois Power of Attorney for Health Care Law (755 ILCS 45/Art. IV) is a legally authorized representative of the principal *(sometimes termed "patient")* who lacks decisional capacity to the extent the written Power of Attorney for Health Care document authorizes the ability to give consent for the treatments or procedures involved in the research and to the extent the agent is complying with the written Power of Attorney for Health Care document and Illinois Power of Attorney for Health Care Law.

3. a "surrogate decision maker" identified by the attending physician pursuant to the Illinois Health Care Surrogate Act (755 ILCS 40) is a legally authorized representative

for a patient who lacks decisional capacity to the extent the surrogate decision maker is complying with the Illinois Health Care Surrogate Act.

NOTE: Legal advice from legal counsel representing the University should be sought regarding the application of this definition to research conducted in other jurisdictions and/or for further clarifications of the above.

Minimal risk. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

NOTE: For research involving people who are incarcerated, 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.

Minor change. A minor change is one in which, in the judgment of the IRB Chair (or designated member), the change itself amounts to merely an administrative change or is an insignificant change in research activities. Minor changes would *not* be those that (1) increase the risk to the human subjects, (2) change the purpose or scientific question of the research project, (3) significantly change recruitment, interaction, intervention, or information gathering activities, (4) alter information given to the human subjects by reducing disclosed risks or adding anticipated benefits, (5) reduce a safeguard or any measure designed to monitor the safety of the human subjects, (6) change the PI, or (7) modify a specific written requirement imposed by the full IRB.

Noncompliance with Policies or IRB Requirements. Any act or omission that violates any provision of this Manual or a requirement imposed by the IRB.

Continuing noncompliance means a situation involving all of the following criteria in sequence:

1. an act or omission that violates any provision of this Manual or IRB requirement;
2. written notice of the noncompliance provided by the IRB to the PI;
3. the passage of a reasonable time period to allow corrective action or avoidance of further noncompliance; and
4. a subsequent and substantially similar act of noncompliance.

Serious noncompliance is an act or omission that is a willful violation and that involves any of the following:

1. knowingly providing false information to the IRB;
2. the development of a clear increased risk of a serious adverse event; or
3. is simply determined by the IRB to be serious.

Nonviable Neonate. A nonviable neonate is a neonate that, although it is living, cannot possibly survive to the point of sustaining life independently, even with the support of available medical therapy. Although it may be presumed that an expelled or delivered fetus is nonviable at a gestational age less than 20 weeks and weight less than 500 grams [Federal Register 40 (August

8, 1975): 33552], a specific determination as to viability must be made by a physician in each instance.

Permission. The agreement of parent(s) or guardian to the participation of their child or ward in research.

Pregnancy. The period from confirmation of implantation of a fertilized egg within the uterus until the fetus has entirely left the uterus (*i.e.*, has been delivered). Implantation is confirmed through a presumptive sign of pregnancy such as missed menses or a positive pregnancy test. This "confirmation" may be in error, but, for research purposes, investigators would presume that a living fetus was present until evidence to the contrary was clear. Although fertilization occurs a week or more before implantation, the current inability to detect the fertilization event or the presence of a newly fertilized egg makes a definition of pregnancy based on implantation necessary.

Pregnant people. A person shall be assumed to be pregnant if they exhibit any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

Principal Investigator (PI). The PI is the individual with primary responsibility and accountability for the appropriate design, conduct, and reporting of the research. A research project may have only one PI. Other investigators of the research project (those who share in the responsibility of the design, conduct, and/or reporting of the research) may exist.

Prisoner. An individual involuntarily confined or detained in a penal institution, including persons: (1) sentenced under a criminal or civil statute; (2) detained pending arraignment, trial, or sentencing; and (3) detained in other facilities (*e.g.*, for drug detoxification or treatment of alcoholism) under statutes or commitment procedures providing such alternatives to criminal prosecution or incarceration in a penal institution.

Public Health Authority. 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 entity acting under a grant of authority from or contract with such 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.

Research. The term “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.

For purposes of this part, the following activities are deemed not to be research:

(1) 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.
(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
(4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

NOTE: For research subject to FDA regulation, the definition differs. The FDA definition (also known as clinical research, clinical study, study, or clinical investigation) is: any experiment that involves a test article and one or more human subjects, and that either:
** must meet the requirements for prior submission to the FDA (i.e. any use of a drug other than use of an approved drug in the course of medical practice OR any activity that evaluates the safety or effectiveness of a medical device) OR*
** need not meet the requirements for prior submission to the FDA, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.*

Research Misconduct. Research misconduct (formerly known as misconduct in science or scientific misconduct) means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. It does not include honest error or honest differences in interpretations or judgments of data. Although the IRB may have a need to know the actions underlying any allegation of research misconduct in performing its functions relating to the protection of human subjects, the procedures regarding to the institutional responsibilities regarding research misconduct are addressed in other University policies and involves the University Research Committee.

Risk. The term "risk" means the probability and magnitude of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study (as distinguished from, for example, the risk of therapies the human subjects would receive even if not participating in the research).

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. For people who are incarcerated, 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.

Physical harm includes exposure to pain, discomfort, or injury from invasive medical procedures, or harm from possible side effects of drugs.

Psychological harm includes undesired changes in thought processes and emotion (*e.g.*, episodes of depression, confusion, or hallucination resulting from drugs, feelings of stress, guilt, or loss of self-esteem).

Social and economic harm includes embarrassment within one's business or social group, loss of employment, or criminal prosecution. Areas of particular sensitivity are information regarding alcohol or drug abuse, mental illness, illegal activities, and sexual behavior.

Serious adverse event. An "adverse event" is any undesirable effect upon a human subject occurring during or within a reasonable time after the conduct of research activities (i.e. the process of intervention or interaction with a human subject and/or the process of collection of identifiable private information about a human subject). An adverse event is "serious" when the undesirable effect is:

1. a physical harm or injury characterized as death, life-threatening condition, in-patient hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect, requires medical or surgical intervention to prevent any of the aforementioned physical harms; or
2. a psychological, social, or economic harm or injury of similar magnitude.

Significant Risk Device. A "significant risk device" is 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 a 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 a subject; or
4. otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

Suspension of approval. Suspension of approval means an action taken by the IRB during a meeting, within the time period in which there is an existing IRB approval in effect, and that fulfills all of the following criteria:

1. is based on a determination that involves either:
   (a) serious or continuing noncompliance with policies or IRB requirements; or
   (b) unanticipated problem involving risk to human subjects or others; and
2. implements a cessation of approval to conduct research activities other than that necessary to protect the rights and welfare of the human subjects as defined by the IRB; and

3. contemplates a potential for approval to be granted upon the occurrence of some event or passage of time as expressed in the IRB determination letter.

Termination of approval. Termination of approval means an action meeting the criteria of "suspension of approval" except that the action does not contemplate approval will be granted in the future (*i.e.* cessation of approval is permanent).

Unanticipated problem involving risk to human subjects or others. The phrase means any incident, experience, or outcome that meets all of the following criteria:

1. unexpected in terms of its nature, its severity, or its frequency (required considerations are what was disclosed during the recruitment process and what was described in the protocol-related documents);
2. related or having a reasonable possibility of being related to the participation in the research (required considerations include whether the sole cause can be identified and what is the natural progression of any pre-existing disease, disorder, or condition); and
3. suggests a greater risk of harm for human subjects or others (in terms of its nature, severity, or frequency of either physical, psychological, economic, or social harm).

Viable Neonate. A viable neonate means one likely to survive to the point of sustaining life independently, given the benefit of available medical therapy. This judgment is to be made by a physician. In accordance with DHHS regulations, the Secretary, HHS, may publish guidelines to assist in the determination of viability. Such guidelines were published in 1975, and specify an estimated gestational age of 20 weeks or more and a body weight of 500 grams or more as indices of fetal viability [Federal Register 40 (August 8, 1975): 33552]. These indices depend on the state of present technology and may be revised periodically.

Vulnerable Populations. Vulnerable populations are those whose constituents, due to some characteristic, condition, or status, are likely to have either diminished decisional capacity or diminished sense of voluntariness (i.e. the exercise of free will relating to whether to give or withhold consent). As a matter of law or University policy, the following are deemed vulnerable populations:

1. pregnant people, human fetuses, neonates or fetal material;
2. people who are incarcerated;
3. children;
4. individuals with impaired decision-making capacity;
5. economically or educationally disadvantaged persons;
6. University students and University employees;
7. any other person, as determined by the IRB, to meet the above definition *(the IRB must consider whether human subject has a pre-existing relationship with the PI or sponsor that involves significant authority, dependence, or fiduciary duties, such as physician-patient, institution-resident, employer-employee, or teacher-student).*

Written or In Writing. Written, or in writing refers to writing on a tangible medium (e.g., paper) or in an electronic format.

APPENDIX C: RESEARCH INVOLVING MEDICAL DEVICES

1. Introduction. In addition to the provisions of this Manual, human subject research involving a medical device shall be reviewed in accordance with this Appendix C.

2. Determination of Significant Risk (SR) or Non-significant Risk (NSR) Device. In human subject research projects that are designed or intended to determine or develop data related to the safety and/or effectiveness of a medical device, a determination must be made whether the medical device is a "significant risk device."

a. If the FDA has made the determination, then that determination is final.

b. If the sponsor has represented that the medical device is a SR device, then an external IRB will be required to review the application.

c. If the sponsor has represented that the medical device is a NSR device, then the IRB shall make an independent determination whether the medical device is a SR or NSR device using *all* the following considerations:

(1) the sponsor's explanation of why it concludes the device is a NSR device;
(2) the regulatory definition of SR (copied in the note below);
(3) the description of the device and how it is to be used in the research;
(4) written FDA guidance (the 2006 guidance is copied within this Appendix C);
(5) any other material that the IRB requests from the sponsor (*e.g.* have other IRBs made a determination about the medical device).

*NOTE: A "**significant risk device**" is 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 a 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 a subject; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.*

3. SR Device Determinations. If the IRB determines the medical device is a SR device, then the IRB shall so notify the PI and sponsor of the determination and the PI and sponsor will be required to use an external IRB for their study.

4. NSR Device Determinations. If the IRB determines the medical device is a NSR device, then further review may be conducted, consistent with this Manual, without an IDE approval. The IRB reserves the right to require review by an external review if they do not have the necessary expertise to review the application.

NOTE: Normally, medical device research will use the full IRB review process. However, it is possible that a NSR device will also be no more than minimal risk and also fulfill the criteria for expedited review. It is important to remember that NSR and no more than minimal risk are different standards.

APPENDIX D: **Humanitarian Use Device**

1. Humanitarian Use Device (HUD). The FDA defines a humanitarian use device as "a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year (Section 3052 of the 21st Century Cures Act (Pub. L. No. 114-255)." To be considered for HUD status, a device sponsor must complete a humanitarian device exemption (HDE) application with the FDA.

    a. The term "use" refers to the use of a HUD for clinical care according to its approved labeling and indication. FDA has decided that a HUD which provides for marketing approval, *does not* constitute "research" or an "investigation."
    b. FDA requires prospective IRB review and approval for clinical use of a HUD.
    c. The IRB does not review HUDs, so any use of HUD at RFUMS would have to be reviewed by an external IRB.

2. Humanitarian Device Exemptions. A humanitarian device exemption is a marketing application for an HUD (Section 520(m) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)). This exemption means that the humanitarian device is exempt from the **effectiveness** requirements of Sections 514 and 515 of the FD&C Act, but is subject to certain profit and use restrictions. The IRB does not review HUDs, so any use of HUD at RFUMS would have to be reviewed by an external IRB.

APPENDIX E: Emergency Research and Emergency use

1. Emergency research refers to the use of FDA regulated products (e.g., drugs, including biological drug products, devices) in emergency settings when an exception from the informed consent requirements is requested under Title 21, Code of Federal Regulations, Section 50.24 (21 CFR 50.24). FDA regulations allow certain planned emergency research to be undertaken when the intervention or interaction will be used with participants who are unable to provide consent because of the emergency situation.
    a. **NOTE.** The IRB does not review planned emergency research, thus no policies are in place for reviewing planned emergency research.
    b. Investigators who wish to conduct planned emergency research should work with the emergency setting's institution that may be willing to provide review and oversight.

2. Emergency use. FDA regulations provide for use of a test article (e.g., drugs, biologics, devices) in 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 56.104(c)).
    a. **Life-threatening**, for the purposes of section 56.102(d), includes the scope of both life-threatening and severely debilitating, defined as:
        i. **Life-threatening** means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.
        ii. **Severely debilitating** means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.
    b. The emergency use of an unapproved investigational drug, biologic or device requires an Investigational New Drug (IND). If the intended recipient 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, biologic or device 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 for treatment of an individual in advance of the IND submission. (21 CFR part 312, subpart I).
    d. Investigators at RFUMS conducting research with FDA regulated products that have been reviewed by an external IRB should follow the external IRB's policies and procedures for emergency use.