Department/Unit: Administration

Policy & Procedure

Original Date: 2/95 Reviewed/Revised: 2/16 Next Review Date: 2/18	**Title** Policy Governing Review and Approval of Human Subject Investigation and Research	Number: 8611-072 Page: 1 of 71 This Policy/Procedure supersedes: 9200-306, 8611-081 9200-302, 9200-029 9200-304

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SECTION 1 - INTRODUCTION

I. Mission

The mission of the NewYork-Presbyterian/Queens (NYP/Q) Institutional Review Board (IRB) is to protect the rights and welfare of human subjects participating in research activities at NYP/Q. The IRB ensures this protection by minimizing risks to subjects while maximizing benefits; In doing so, the designated IRB must ensure that human subject research is conducted ethically, and in compliance with Federal regulations, the requirements of applicable New York State and local law, NYP/Q's Assurance, and NYP/Q's policies and procedures. The designated IRB fulfills these responsibilities by conducting prospective and continuing review of human subject research, including review of the protocol, the informed consent process, procedures used to enroll subjects, as well as any adverse events or unanticipated problems reported to the IRB. Prospective review and approval of research or changes to previously approved research ensures that research is not initiated without IRB review and approval. In its communications to investigators, the IRB makes investigators aware of the requirement to submit changes to the IRB for review and approval before initiation except where necessary to eliminate apparent immediate hazards to the subject.

Scope of the IRB's Authority. All human subject research conducted at NYP/Q or by NYP/Q's employees or agents, whether at NYP/Q or at other sites, whether by themselves or with collaborators at other sites, must be prospectively reviewed and approved by the NYP/Q IRB or an IRB designated by NYP/Q. The Western Institutional Review Board (WIRB) is an independent commercial IRB contracted by NewYork-Presbyterian/Queens to review, approve and monitor the institution's industry sponsored and federally funded human subjects' research, and such other research as may be determined from time to time by the IRB Administrator. WIRB complies with NYP/Q policies and reviews research in accordance with Federal Regulations. Although WIRB serves as the IRB of record for the industry and federally sponsored studies all active research is subject to NYP/Q policies and procedures and standard operating procedures related to conduct of all research at the institution. Determination of eligibility for WIRB Review will be made by the Staff at the Lang Center for Research and Education (Director of the Center, IRB Administrator). No human subject research may be initiated or continued at NYP/Q or by NYP/Q's employees or agents without prospective approval of a designated IRB.

The ultimate responsibility for the IRB resides with the Institutional Official (IO) of the NYP/Q human research protection program. The IO is legally authorized by NYP/Q to represent the institution on all matters pertaining to human research protections and ensures that the IRB has the resources and support necessary to comply with all organizational policies, laws, and regulations that govern human subject research. The IO is the signatory on NYP/Q's Assurance of Compliance (FWA) to the federal government and assumes the obligations of the FWA.

NYP/Q IRB and WIRB are empowered to take any action necessary to protect the rights and welfare of human subjects in research conducted at NYP/Q or by NYP/Q's employees or agents. NYP/Q IRB and WIRB have the authority to approve, require modifications in, or disapprove any human subject research conducted at NYP/Q or by NYP/Q's employees or agents.
NYP/Q IRB and WIRB may suspend or terminate the enrollment and/or ongoing involvement of human subjects in NYP/Q's research as it determines necessary for the protection of those subjects, especially in instances of serious or continuing noncompliance. WIRB has the authority to observe, monitor, and/or audit NYP/Q's human subject research to whatever extent it considers necessary to protect human subjects and assure compliance with applicable laws and regulations. In cases of serious or continuing noncompliance, both NYP/Q and WIRB may: (i) disqualify an investigator from conducting a particular research project or research altogether at the institution; (ii) require education and training in the ethics and regulation of human subject research; or (iii) any other reasonable measure deemed appropriate to protect the rights and welfare of research subjects.

II. Subject of Policy & Procedure

All research activities that involve (1) the collection of information through intervention, interaction with, or observation of individuals or (2) the collection or use of private information about individuals, must be evaluated to determine if the project (a) does not constitute human participant research, (b) constitutes human participant research but eligible for exemption from IRB review, or (c) must be submitted to the Institutional Review Board for Human Participants (IRB) for review and approval. See Appendix A for definitions that will help determine if IRB review is required. When in doubt, investigators should call the Lang Center.

III. What is Affected by this Policy & Procedure

The following policy shall govern the review and approval of human subject investigation and research by any individual in the confines of NewYork-Presbyterian/Queens (NYP/Q). Pursuant to this policy, the Medical Center's Board of Trustees has delegated to the Medical Center's Institutional Review Board (IRB) the authority to review and pass on any request for clinical investigation and research involving human subjects in the hospital, or to refer the research to a designated external IRB. This Policy & Procedure applies to all past, on-going and future human participant research projects being conducted by NYP/Q faculty, residents, fellows and staff.

IV. Definitions

See **Appendix A.**

V. Regulations and Guidance Applicable to Human Participant Research Determinations

Federal regulations pertaining to human participant research state explicitly that they do not affect state laws which may otherwise be applicable and which provide additional protections for human participants. See 45 CFR § 46.101(f) (http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.101).

A. New York State Laws Addressing Human Participant Research Issues

New York State Public Health Law Article 24-A. Protection of Human Subjects

New York State addresses research involving human participants in Public Health Law Article 24-A. *Protection of Human Subjects.* New York State expressly exempts federally funded research from compliance with Public Health Law Article 24-A: "The provisions of this article shall not apply to the conduct of human research which is subject to, and which is in compliance with, policies and regulations promulgated by any agency of the federal government for the protection of human subjects." § 2445.

i. Issues of Informed Consent

Age of Majority: Under the federal Common Rule, "children are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted" (45 CFR § 46.402). In New York State, a "minor" is defined as a person who is under eighteen (18) years of age (Chapter 14, Domestic Relations Law, Article 1, § 2).

Parent: New York State defines "parents" according to the law at issue. The term parent is not defined in Public Health Law Article 24-A concerning human subjects protection. At a minimum, however, the term parent means father or mother by birth or adoption.

Legal Guardian**:** Under the federal Common Rule, "guardian means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care" (45 CFR § 46.402(e)). Moreover, "legally authorized representative means 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" (45 CFR § 46.102(c)).

In New York State, Legal Guardian is defined as an individual who has obtained legal guardianship through:

1. Surrogate Courts Proceedings Act §17. *Guardians and Custodians*
2. Domestic Relations Law §81. *Appointment of Guardians by Parent*
3. Article Six of the Family Court Act, addressing *Guardianship, Adoption, Custody*

ii. Research Conducted outside New York State: It is the Principal Investigator's responsibility to determine which individuals are considered "children" or "guardians" outside of New York State. The Principal Investigator should incorporate compliance with New York State Law into the consent process.

iii. HIV Testing: Unless federal law authorizes otherwise, NYS law requires written informed consent to testing for HIV from a test subject with capacity to consent or, if lacking, of a person authorized pursuant to law to consent to health care for such individual (i.e., legally empowered parent or guardian). Public Health Law § 2781(1), complete consent requirements: (http://public.leginfo.state.ny.us/menugetf.cgi?COMMONQUERY=LAWS).

However, written informed consent is not required "for the purpose of research if the testing is performed in a manner by which the identity of the test subject is not known and may not be retrieved by the researcher" (Public Health Law § 2781(6)(b)).

B. Federal Regulations Addressing Human Participant Research Issues

Every institution that receives funds from DHHS must have an "Assurance" of protection for human subjects (45 CFR 46.103). NYP/Q currently conducts human subject research under a DHHS, OHRP-approved Federal wide Assurance (FWA). NYP/Q IRB has a

Federal wide Assurance (FWA) with the Office for Human Research Protections (OHRP) of the U.S. Department of Health & Human Services which guarantees its application of the federal policy for the protection of human participants in 45 CFR 46 and its Subparts A, B, C, and D, when engaging in human participant research.

Federal regulations require specific protections for human subjects. DHHS regulations at 45 CFR Part 46, Subpart A constitutes the Federal Policy (Common Rule) for the Protection of Human Subjects. The DHHS regulations also include additional protections for pregnant women, fetuses and neonates (Subpart B), prisoners (Subpart C), and children (Subpart D). All human subject research at NYP/Q must comply with all four Subparts of the DHHS regulations. These regulations are enforced by the DHHS, Office for Human Research Protections (OHRP). These regulations apply to all human subjects research conducted at NYP/Q.

FDA has codified informed consent (21 CFR Part 50), IRB (21 CFR Part 56), and child protection (61 FR 20589 and 21 CFR Part 50, Subpart D) regulations that are almost identical to the DHHS regulations. Additional FDA regulations relevant to the protection of human subjects address Investigational New Drug Applications (21 CFR Part 312), Biological Products (21 CFR Part 600), and Investigational Device Exemptions (21 CFR Part 812). In general, FDA human subject regulations apply to clinical investigations and other research involving products regulated by FDA, including food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. IRB review and approval is required for clinical investigations and other research involving products regulated by FDA for human use, even where an Investigational New Drug Application (IND) or Investigational Device Exemption (IDE) is not required.

VI. Ethical Codes Addressing Human Participant Research Issues

- The Nuremberg Code (1948) - **Appendix B**
- The Belmont Report (1974) - **Appendix B**
- Declaration of Helsinki (last revised in 2000) - **Appendix B**

VII. IRB Record Keeping & Required Documentation

In accordance with Federal regulations at 45 CFR 46.115(b), IRB records will be retained by NYP/Q for no less than three years, and Individual Investigator's research records will be retained by the Investigator for no less than three years after the completion of the research. All IRB records will be kept secure in locking filing cabinets. Inactive files will be secured in an off-premises, archival storage facility.

Written minutes shall be prepared for all IRB meetings. The minutes shall include: (1) attendance at the meeting; (2) actions taken by the IRB; (3) the IRB vote on the actions taken, including indication of any dissenting votes or abstentions; (4) description of the substance of the discussion of each protocol; (5) a summary of discussion of controverted issues and their resolution; (6) IRB findings regarding waiver or alteration of informed consent requirement; (7) IRB findings regarding waiver of the requirement for written consent documents; (8) IRB findings with regard to added protection for children when serving as research subjects; (9) indication when members have conflicting interest regarding a project and their absenting themselves from the discussion under such circumstance; (10) the basis for requested changes in research proposals or consent documents or for disapproval of research proposals; (11) the IRB determination as to the handling of responses to requests for information or revisions in protocol or consent documents; (12) substance of discussions of reports of adverse reactions; (13) substance of discussions of allegations of non-compliance

with human subjects regulations; (14) substance of discussions of suspension of a research project and the reasons for which the action was taken; (15) summary of other discussions or actions of the IRB.

VIII. Review by Institution

Research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB.(45.46.112)

SECTION 2 - THE SCOPE, PURPOSE AND RESPONSIBILITY OF THE INSTITUTIONAL REVIEW BOARD (IRB)

I. Purpose of the IRB

A designated IRB's primary responsibility is to ensure that the rights and welfare of subjects are protected in human subject research. In doing so, the designated IRB must ensure that human subject research is conducted ethically, and in compliance with Federal regulations, the requirements of applicable New York State and local law, NYP/Q's FWA, and NYP/Q's policies and procedures. The IRB fulfills these responsibilities by conducting prospective and continuing review of human subject research, including review of the protocol and grants (for Federally-funded research), the informed consent process, procedures used to enroll subjects, as well as any adverse events or unanticipated problems reported to the IRB. Prospective review and approval of research or changes to previously approved research ensures that research is not initiated without IRB review and approval.

II. Responsibilities of the IRB

The IRB will comply with this policy and all regulations promulgated by federal and state regulatory bodies and agencies; shall meet as often as necessary to perform its duties, but at least four times a year; shall maintain a permanent record of its findings, proceedings and actions; and shall make reports and recommendations to the Board of Trustees as well as the Medical Board and the Chief Executive Officer, as appropriate and upon request.

The IRB will ensure prompt reporting to appropriate institutional officials, the FDA and the IRB of: (i) any unanticipated problems involving risks to human subjects or others (ii) any instances of serious or continuing noncompliance with federal regulations or the requirements or determinations of the IRB, or (iii) any suspension or termination of IRB approval.

Each member of the IRB shall be entitled to one vote on matters that appropriately come before the body for action and a majority of the members present must vote favorably to approve an action. A quorum, consisting of a simple majority of the members of the IRB, must be met and maintained for convened meetings.

The IRB Office staff assigns a primary and secondary reviewer for all protocols requiring initial full review. A primary reviewer is assigned for continuing full review and for all protocols requiring full review of modifications to previously approved research. When making reviewer assignments, IRB Office staff will assign a member or members of the IRB, and will take into consideration the vulnerable populations involved in the research and the expertise required to review the research. Prior to the convened IRB meeting, each project is reviewed in depth by the assigned reviewer(s).They are expected to have reviewed all provided material in order to have a meaningful discussion of the presented information during the convened IRB meeting.

At the meeting, the Primary and Secondary Reviewers present an overview of the goals, design, study procedures, safety procedures, and qualifications of the investigators. The

Primary and Secondary Reviewers, will then complete the reviewer's regulatory/criteria checklist to identify the appropriate type of review.

III. Scope of the IRB's Authority (see Mission or IRB;p. 2)

Only current appointees to the Attending Medical Staff of NYP/Q who have been granted appropriate clinical privileges may apply for approval of a proposed investigational drug, diagnostic test or device to be used in research projects involving human subjects; non-Medical Staff may conduct research not using investigational drug or diagnostic test or device (e.g. surveys, chart reviews, etc.). All human subject research conducted at NYP/Q must be prospectively reviewed and approved by the either the NYP/Q IRB or a designated IRB (WIRB). No human subject research may be initiated or continued at NYP/Q without prospective and continuing approval of the NYP/Q IRB or a designated IRB (WIRB).

Department Chairperson or Head of an Institute, Center, or Division.

Each Chairperson or head of an academic Department Institute, Center, or Division shall be responsible to the NYP/Q IRB for the supervision and proper conduct of research involving human subjects in his or her Department, Institute, Center, or Division in accordance with the procedures prescribed by the NYP/Q IRB or the designated IRB. Thus, before a protocol can be sent to the IRB for review, it must be approved by the departmental Chairperson or Institute Head or Center or Division Head when applicable, and by the Chief of the Division of the Principal Investigator (PI).

IV. IRB Membership

In compliance with Federal regulations at 45 CFR 46.107, NYP/Q's IRB must satisfy the following requirements: (i) The IRB will have at least seven members. (ii) IRB members will possess varying backgrounds to promote complete and adequate review of research activities commonly conducted at NYP/Q. (iii) IRB members will be sufficiently diverse relative to race, gender, cultural background, and sensitivity to community attitudes so as to promote respect for the IRB's advice and counsel in safeguarding the rights and welfare of human subjects. (iv) IRB members will include persons able to ascertain the acceptability of proposed research in terms of institutional commitments, regulations, applicable law, and standards of professional conduct and practice. (v) The IRB will consist of qualified persons of both sexes. (vi) The IRB will not consist entirely of members of one profession. (vii) The IRB will include at least one member whose primary expertise is in a scientific area. (viii) The IRB will have at least one member whose primary concerns are in non-scientific areas. (ix) The IRB will include at least one member who is not otherwise affiliated with NYP/Q and who is not part of the immediate family of a person who is affiliated with NYP/Q

NYP/Q IRB will have sufficient expertise to review the broad variety of research in which NYP/Q commonly becomes involved, will be knowledgeable about all relevant regulatory requirements, and will remain impartial and objective in its reviews. An IRB Administrator shall oversee the duties and activities of the IRB. The President and Chief Executive Officer in consultation with the IO, and Chairperson of the Medical Board, shall recommend the names of individuals who fulfill the qualifications specified in this policy to the Chairperson of the Board of Trustees for consideration. Members and Alternates shall be appointed by the Chairman, after consultation with the CEO, with the consent of the Board of Trustees, and shall serve at the pleasure of the Board of Trustees.

V. Initial Training and Continuing Education of IRB Members

Upon receiving an appointment to the IRB, a member receives comprehensive reference materials (including these operating procedures) necessary to review research from an ethical and regulatory perspective. Additionally, each IRB member and alternate must undergo an orientation that assure the institution and the Department of Health and Human Services that

required human subject research training/instruction (CITI Program) has been obtained prior to any research protocol review/approval. Certificates of completion are maintained by the office of the IRB. Continuing education is required every two years. IRB member must also complete a Financial Disclosure Form (**Appendix C**) which will be maintained by the IRB office. Members and alternates will periodically be provided with education materials.

VI. Local Research Context

Federal guidance requires that an IRB consider the local research context in reviewing research proposals. Federal regulations at 45 CFR 46.107(a) further require that IRB's be (i) sufficiently qualified through the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its counsel; and (ii) able to ascertain the acceptability of proposed research in terms of the institutional commitments and regulations, applicable law, and standards of professional conduct and practice.

In accordance with this obligation, and when appropriate, an IRB member shall serve as the local representative. In the absence of an appropriate IRB member to serve as local representative, NYP/Q IRB shall obtain a written review of the Investigators report of the local research context from one or more appropriate local representatives, in conjunction with participation of the local representative as a guest in convened meetings of the IRB, when such participation is deemed warranted by either the local representative or by any member of the IRB (for example, if the project involves gene transfer or a vulnerable subject population).

VII. Quorum

A Convened IRB meeting is one at which a quorum is present (or participating via teleconference), which means that a majority (more than half) of the members of the IRB are present, including at least one member not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution. For studies that are FDA-regulated, the quorum must include at least one physician. Members attending by telephone- or video-conference count towards the quorum and may vote providing they have received all pertinent material prior to the meeting and they can participate actively and equally in the discussion of the protocols. The IRB minutes should document that these two conditions are met. The IRB Administrator will confirm that an appropriate quorum is present and convey that information to the IRB Chair. The IRB Administrator and Chair will be responsible in ensuring that the IRB meetings remain appropriately convened.

Members vote to approve, require modifications in, disapprove, or defer research submitted to the IRB. Members are expected to attend IRB meetings on a regular basis and serve as general reviewers on all research discussed at convened meetings. *Alternate IRB Members* are to replace regular IRB members who are, on occasion, unable to attend convened meetings of the IRB. Alternate members must be listed on the IRB's official membership roster, which must specify which member (or members) the alternate is qualified to replace. (Note: Although an alternate may be qualified to replace more than one regular member, only one such member may be represented by the alternate at any convened meeting.) *Consultants*, at the discretion of the IRB, individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB may be invited. These individuals may not vote with the IRB.

A quorum can fail during a Convened meeting, by, among other things, loss of a majority through recusal of members with conflicts of interest, early departures, or the absence of a non-scientist member. In the case of quorum failure, the remaining group may continue discussion of protocols, but may not take further actions unless and until the quorum can be

restored. All members present at a convened meeting have full voting rights, except in the case of a conflict of interest or if both a voting member and an Alternate is present. In that instance, the Voting member will be counted toward the quorum. In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting.

SECTION 3 - REQUIREMENTS FOR ALL INDIVIDUALS INVOLVED IN RESEARCH ACTIVITIY

(IRB MEMBERS, IRB STAFF, PRICIPAL INVESTIGATORS, KEY PERSONNEL, RESEARCH ASSISTANTS, VOLUNTEERS)

I. Human Subject Protection Education Program for All Personnel Involved in Research

NYP/Q is required to have a plan to provide education about human subject protections for research investigators and their key personnel as well as IRB members and staff. The IRB office is responsible for developing and implementing this education plan. The IRB has identified the CITI Program – Course for the Protection of Human Subjects developed by the University of Miami as the preferred course. All investigators, key personnel and other persons identified on the research protocol are responsible for successfully passing the exam. Initial certification is valid for 3 years from the date of completion; re-certification is required at 3 year intervals in order for all key personnel to participate in research at NYP/Q. The course can be found at https://www.citiprogram.org.

Before the IRB can release the determination of a review, the Protocol PI, all co-investigators, and all key personnel must successfully complete the IRB online training (https://www.citiprogram.org) addressing the appropriate conduct of human participant research. Proof of completion of this requirement by all investigators and key personnel must be submitted to the IRB.

II. Financial Disclosure

A. IRB Members

All IRB members must complete a Financial Disclosure Form (**Appendix C**), which will be kept in a secure location in the IRB office. If any real or perceived financial conflict of interest existed, this information will be forwarded to the Vice President of Regulatory Affairs for further determination. If an IRB member has any real or perceived financial conflict of interest, the member must abstain from voting on or monitoring any applicable research project. It is the responsibility of the IRB member to update/inform the IRB Administrator of any new information that may create a potential conflict.

No IRB member may participate in the IRB's initial or continuing review of any project in which the member has any real or perceived financial conflict of interest, except to provide information requested by the IRB. IRB members, including the Chairperson, who have conflicting interests are required to disclose such interests and to recuse themselves from deliberation and voting on the relevant protocol. Such absences are recorded in the meeting's minutes.

B. Investigator and Key Personnel

Prior to initiation of the research, a Financial Disclosure Form (**Appendix C**) must be completed by all research investigators and key personnel and submitted to the offices of the Institutional Review Board. If any real or perceived financial conflict of interest existed, this information would be forwarded to the Vice President of Regulatory Affairs to determine how the conflict, if any, will be managed, reduced or eliminated

If any real or perceived financial conflict of interest existed, the Vice President of Regulatory Affairs must inform the IRB to determine how the potential conflict should best be managed; including what modifications might need to be made to the protocol and/or to the consent form. All financial conflicts of interest that directly affect research must be managed, reduced or eliminated

For any research sponsored by the Federal Government, the investigative team (defined as anyone responsible for the design, conduct or reporting of research) must review all regulations regarding financial conflicts of interest relating to federally funded research; and all requirements/responsibilities must be adhered to. It is the responsibility of the investigative team to update/inform the IRB Administrator of any new information that may create a potential conflict.

C. IRB Staff
All IRB Staff must complete a Financial Disclosure Form (**Appendix C**), which will be kept in a secure location in the IRB office If any real or perceived financial conflict of interest existed, this information will be forwarded to the Vice President of Regulatory Affairs for further determination. If an IRB staff member has any real or perceived financial conflict of interest, the Vice President of Regulatory Affairs will determine the best course of action

SECTION 4 - DETERMINATION OF WHETHER AN ACTIVITY NEEDS IRB REVIEW OR EXEMPTION

I. For Research Activities that do not Constitute Human Participant Research

A. Responsibilities of the Protocol Principal Investigator(PI)
If the Protocol Principal Investigator is unsure if their research activity constitutes human participant research, they should contact the IRB Administrator to make the preliminary determination. If the research activity does not involve human participant research, the Administrator will advise the Investigator of such. However, for each change that is proposed or occurs during the execution of the research activity, the Protocol PI may need to re-consult the IRB Administrator to determine whether that change affects the need for review and approval by the IRB or a determination by the IRB Administrator of exemption from IRB review.

B. Responsibilities of the IRB Administrator
If the IRB Administrator makes a preliminary determination that the research activity does not constitute human participant research, the Protocol PI will be notified by email or memorandum that the research activity does not involve human participant research and, thus, does not require IRB review and approval or an exemption from IRB review. The Protocol PI is required to maintain this notification for a period of three years after the research activity has concluded and all publication and/or reports have been accepted. (See Introduction Section: IRB Record Keeping) =

II. For Research Activities that do Constitute Human Participant Research

A. Responsibility of the Protocol Principal Investigator
If the Protocol PI or the IRB Administrator determines that the research activity *does* involve human participant research, the Protocol PI will complete and submit to the IRB Administrator for processing an Institutional Review Board Application for Initial and Expedited Review (**Appendix D**) or an Application for Exempt Determination (**Appendix**

M) and all other materials required for review. (See Section 5 - IRB Review Process/Possible Outcomes/ Minimal Requirements for Approval by the IRB)

B. Responsibilities of the IRB Administrator for Research Activities that are Eligible for Exemption from IRB Review (See Section 4 - IRB Process for IRB Exemption Status; Section 4A:Determining Research Eligible for Exemption from IRB Review)
If the IRB Administrator makes the preliminary determination that the research project is human participant research but eligible for Exemption from IRB review the IRB Administrator will forward the project to an IRB board member for review. Upon receipt of granted exemption, the IRB Administrator will issue a formal notice of exemption covering the duration of the project to the Protocol PI. For each change that is proposed or occurs during the execution of the research activity, the Protocol PI may need to consult with the IRB Administrator to determine if the change affects the eligibility of the research activity to continue to be exempt from IRB review and approval. A copy of this notice and all submission documents will be archived by the IRB Department until three years after the termination of the research activity. In addition, the Protocol PI should maintain these documents for a period of three years after the research activity has concluded and all publication and/or reports have been accepted. (*See* Introduction Section: IRB Record Keeping).

C. Responsibilities of the IRB Administrator for Research Activities that Require IRB Review and Approval
For research activities that are determined to require IRB review and approval, the IRB Administrator and/or the Director of the Lang Research Center shall conduct a preliminary review of all research protocol application materials for (a) *completion* and (b) *the need for the Protocol PI, all co-investigators, and key personnel to complete training in the use of human participants in research.* (All requirements under Section 2) After it has been determined that the research protocol application is complete, it will be submitted to the IRB for their review and approval via the Expedited Review Process or the Convened Committee Review Process. (See Section 4- IRB Review Process/Possible Outcomes/ Minimal Requirements for Approval by the IRB for further instructions).

SECTION 5 - IRB REVIEW PROCESS/POSSIBLE OUTCOMES/MINIMAL REQUIREMENTS FOR APPROVAL BY THE IRB (NYP/Q IRB or designated IRB)

Note: No research activity shall be initiated until the Protocol PI has received written notification from the IRB Administrator that the protocol has been "approved" by the IRB.

I. Role of IRB in Review and Approval of Human Participant Research Before its Initiation:

In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting (45 FR46.108(b).

Except when an expedited review procedure is used, the IRB will review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research

to be approved, it must receive the approval of a majority of those members present at the meeting.

The IRB evaluates each protocol application to assess the risk/benefit ratio and the methods used by the principal investigator and the research staff for protecting the rights of the research participants while allowing the research data to be collected for the benefit of society.

In making this assessment, the IRB will examine the initial protocol application, which will consist of the protocol itself, along with the following applicable items: recruitment materials, consent documents or waivers, 1572 forms, Investigator Drug Brochures, Investigator Device Brochures, and any other supporting documents. The IRB will also consult the Protocol PI, as necessary, to gather additional information.

The goal of IRB review is to ensure approval only of research projects that, at minimum, meet the criteria listed in Section 4B: delineating the parameters for adequate protection of the rights and welfare of human participants, as derived from (1) federal and state laws, (2) federal and state regulations, and (3) the principles of justice, beneficence, and autonomy articulated in applicable ethical codes like the Belmont Report and the Declaration of Helsinki.

II. Minimal Requirements for IRB Approval of Research

Federal regulations at 45 CFR 46.111, FDA regulations at 21 CFR Part 56, and the Federal Policy (Common Rule) delineate specific criteria for the approval of research. IRB's designated by NYP/Q will determine that all of the following requirements are satisfied before approving proposed research.

Before approving a research proposal the IRB shall determine that the following requirements are satisfied:

(a) Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

(b); Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(c) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

(d) that informed consent will be sought from each prospective subject or subject's legally authorized representative in accordance with 45 CFR 46.116 and 21 CFR 50.25;

(e) that informed consent will be appropriately documented in accordance with 45 CFR 46.117 and 21 CFR 50.27;

(f) that the research plan appropriately monitors the data collected to insure the safety of subjects;

(g) that subject's privacy is appropriately protected and confidentiality of subject related data maintained;

(h) that appropriate additional safeguards are included to protect the rights and welfare of subjects who are likely to be vulnerable to coercion

The IRB will also take into consideration that the principles of justice, beneficence, and autonomy articulated in applicable documents such as GCP, the Belmont Report and the Declaration of Helsinki are met.. No research activity shall be initiated until the Protocol PI has received written notification from the IRB Administrator that the protocol has been "approved" by the IRB.

III. Possible Outcomes from an IRB Review

IRB minutes will include all actions taken by the IRB and the votes underlying those actions. The reviewers will complete and submit the Primary Initial Review checklist and the Secondary Initial Review checklist. These actions will also be provided in writing to investigators in the form of a memorandum from the IRB. IRB actions for review of research include the following:

A. Approved with no changes: Once an official IRB approval letter is received, the project may begin.

B. Approved with modifications: These include specifically stipulated minor changes that are required, which can be reviewed by the IRB Chairperson or by a designated IRB member. Such stipulated changes must be clearly delineated by the IRB so the investigator may simply concur with the IRB's stipulations. The research may proceed after the required changes are verified by the IRB Chairperson or designated reviewer.

If the project is approved with modifications the following will occur:

- The IRB Office informs the investigator/sponsor in writing of the IRB's decision.
- If applicable, the investigator's/sponsor's response is sent to the IRB Office for review through Expedited Review.
- Once an official IRB approval letter is received, the project may begin.

For projects that have been approved with modifications, the effective date of the IRB's approvals starts on the date of the secondary (expedited review) approval.

C. Deferred

The IRB determines that it lacks sufficient information about the research to proceed with its review. The research may not proceed until the convened IRB has approved a revised application incorporating all necessary information. Any changes that were required by the IRB must be reviewed by the convened IRB. Any requested changes, which are not specifically stipulated will be treated as substantive, and response will be reviewed by the convened IRB.

If the project is deferred the following will occur:

- The IRB Office informs the investigator/sponsor in writing of the IRB's decision.
- The investigator's/sponsor's response is sent to the IRB Office.

- In order to receive approval for a deferred project, it must be submitted for full IRB review at a subsequent, convened meeting of the same IRB. The IRB Office will provide to the IRB members the investigator's response, the revised protocol and/ or consent with highlighted changes, all original submission materials. The amended protocol application is given full IRB review.
- The Investigator will be notified of the IRB's determination.

D. Disapproved

The IRB has determined that the research cannot be conducted as written, at NYP/Q, or by employees or agents of NYP/Q. The IRB Office informs the investigator/sponsor in writing of the IRB's decision. The principal investigator has the option to appeal the IRB's decision or submit a new protocol to the IRB as a new submission. If the Investigator chooses to appeal the IRB's decision and the decision is upheld, the project cannot be re-reviewed. It must be revised and submitted as an entirely new project.

IV. Reporting IRB Actions

All IRB actions are communicated in writing within 14 working days of the IRB's determination. When approving a protocol, the IRB will forward official notification with a copy of the approved consent form and any other subject materials (if applicable). The approval will convey the IRB's date of approval and expiration. When deferring a protocol, the IRB notification will include the modifications required for approval along with the reasoning for requiring such modifications. When disapproving, terminating or suspending a protocol, the IRB notification will include the reasoning behind such decision.

All Correspondence will be maintained by the IRB and the PI in accordance with the Introduction Section: IRB Record Keeping & Required Documentation

V. Appeal of IRB Determinations

No NYP/Q committee or official may set aside or overrule a determination by the IRB to disapprove or require modifications in human subject research. The IRB will provide the investigator with a written statement of its reasons for disapproving or requiring modifications in proposed research and will give the investigator an opportunity to respond in person or in writing. The IRB will carefully and fairly evaluate the investigator's response in reaching its final determination.

VI. Research Conducted Without IRB Approval

NYP/Q IRB has a Federalwide Assurance (FWA) with the Office for Human Research Protections (OHRP) of the U.S. Department of Health & Human Services guaranteeing its application of the federal policy for the protection of human participants in 45 CFR 46 and its Subparts A, B, C, and D, when engaging in human participant research.

Investigators are responsible for obtaining IRB approval before beginning any nonexempt human subjects research (45 CFR 46.109(a) and (d)). Investigators are responsible for providing the IRB with sufficient information and related materials about the research (e.g., grant applications, research protocols, sample consent documents) so that the IRB can fulfill its regulatory obligations, including making the required determinations under 45 CFR 46.111 and, if applicable, subparts B, C and D. Investigators should follow institutional policies and procedures for IRB review that are required by HHS regulations at 45 CFR 46.103(b)(4)

If the IRB determines or has reason to believe that any physician or other practitioner is conducting research in the Medical Center without the approval of the IRB or beyond the scope of the IRB's approval, the IRB shall order the physician or other practitioner to stop the research immediately. As the IRB may not approve research retroactively, the PI must submit to the IRB an explanation for why s/he thought that IRB approval was not required. Based on the information provided, the IRB will conduct an inquiry and determine the extent of noncompliance, whether the research was conducted ethically, and whether the data may be utilized. Additionally, the IRB will refer this matter to the Medical Director and Chief Executive Officer for possible additional action.

VII. Suspension or termination of IRB approval of research.

An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head (45.46.113)

All investigators conducting research at NYP/Q or as employees or agents of NYP/Q are required to notify the IRB promptly of any serious adverse events or unanticipated problems involving risks to subjects or others. In addition, all employees and agents of NYP/Q are required to notify the IRB promptly of any serious or continuing noncompliance with applicable regulatory requirements or with the determinations of the IRB. The convened IRB may vote to suspend or terminate approval of research not being conducted in accordance with IRB or regulatory requirements or that has been associated with unexpected problems or serious harm to subjects. The IRB will notify the principal investigator in writing of such suspensions or terminations and will include a statement of the reasons for the IRB's actions. The investigator will be provided with an opportunity to respond in person or in writing. Where the IRB Chairperson determines that such action is necessary to protect the rights and welfare of subjects, the Chairperson may require an immediate, temporary suspension of enrollment of new subjects or of continued participation of previously enrolled subjects, pending review of the situation by the convened IRB. It is the responsibility of the IRB Chairperson to promptly notify relevant Federal Agencies, including OHRP and FDA (for FDA regulated research) of the suspension or termination.

VIII. Review in Emergency Situations

Federal regulations do not permit research activities to be started, even in an emergency, without prior IRB review and approval except as described below. When emergency medical care is initiated without prior IRB review and approval, the patient may not be considered a research subject. Such emergency care may not be claimed as research, nor may any data regarding such care be included in any report of a prospectively conceived research activity.

IX. Emergency Use of a Test Article without IRB Review

Emergency use is defined as the use of an investigational drug or biological product (a "test article") with a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain NYP/Q IRB approval. The exception, which may not be used unless both conditions exist, allows for one emergency use of a test article. The IRB must then be notified before or within five days of the actual emergency use of the test article. Regulations require that any subsequent use of the investigational product at the institution have prospective NYP/Q IRB review and approval.

An exemption under FDA regulations at 21 CFR 56.104(c) permits the emergency use of an investigational drug, device, or biologic on a one-time basis per institution without IRB review and approval. All of the following conditions must be met for this type of emergency use:

- A human subject is in a life-threatening situation
- No standard acceptable treatment is available
- There is insufficient time to obtain IRB approval
- The emergency use must be reported to the IRB within five working days

The investigator must obtain the informed consent of the subject for such an emergency use.

SECTION 6 - OFF LABEL (UNAPPROVED) USE OF FDA-REGULATED PRODUCTS IN MEDICAL PRACTICE VS. RESEARCH

Good medical practice and the best interests of the patient require that physicians use legally available, marketed drugs, biologics and devices according to their best knowledge and judgment. If physicians use a product for an indication not included in the approved labeling (i.e. off-label), they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence, and to maintain records of the product's use and effects. Off-label use of a marketed product in this manner when the intent is solely the practice of medicine does not require IRB review or the submission of an IND or IDE. Off-label use of a marketed product in research (i.e. as part of a systematic investigation designed to develop or contribute to generalizable knowledge) does require IRB review. Off-label use of a marketed product intended to support a change in labeling requires both IRB review and submission of an IND or IDE.

SECTION 7 - PROCEDURES FOR SUBMISSION OF NEW PROJECTS FOR EXPEDITED REVIEW OF RESEARCH

Upon receipt of the research protocol and supporting documents, the IRB Administrator will (1) make a preliminary determination that the research activity constitutes human participant research; (2) verify the completeness of the materials or coordinate with the Protocol PI to achieve completion; (3) make a preliminary review of the protocol and attached materials to determine whether the Expedited or Convened Committee process is appropriate; (4) enter selected information from the Institutional Review Board Application for Initial and Expedited Review (**Appendix D)** into IRB Manager database; and (5) determine the need for all investigators and key personnel to complete training in the use of human participants in research.

A preliminary review of all applications will be done by the IRB Administrator upon receipt; incomplete applications will be returned to the Protocol PI for follow-up. The protocol shall include: a complete description of the research procedures and methods to be employed; the background to the proposed research; the current state of knowledge in the field; the significance of the research proposed; all risks to the subjects which can be anticipated as a consequence of their participating in the research; procedures to be employed to minimize risks to subjects; any benefits to the subjects which might reasonably be expected from their participation in the study; procedure for obtaining informed consent and informed consent document; nature of the research subject population, including sex, age, racial and ethnic characteristics; procedures for recruiting subjects; number of subjects to be studied; alternative procedures for diagnosis and/or treatment and their benefits and risks; procedures to be employed to maintain confidentiality of patient related data; source of funding to support the research; financial compensation, if any, for the research subjects.

Only the IRB Administrator, the Chair of the IRB, or an experienced IRB reviewer who has been designated by the Chair of the IRB may make the determination that a submission is eligible for Expedited Review.

An IRB member with relevant expertise will be selected by the IRB Administrator or the Chair of the IRB as an Expedited Reviewer. The Expedited Reviewer will complete the Primary Initial Review checklist and the Secondary Initial Review checklist and return it to IRB Administrator. The IRB Administrator will email the Expedited Reviewer's comments, questions, and/or suggestions for revisions to the Protocol PI, who will respond in writing to IRB Administrator. The response will be reviewed by the Expedited Reviewer or the Chair of the IRB. These communications may continue until the Expedited Reviewer or the Chair of the IRB approves the protocol or refers the protocol for review by the Convened IRB.

The Expedited Reviewer(s) may exercise all of the decisional authorities of the IRB, except that Expedited Reviewer(s) may not disapprove the research protocol. The Expedited Reviewer(s) may approve, require specific minor revisions, or refer the research to the Convened IRB for review and approval. If there are concerns about whether or not an individual research project meets the definition of minimal risk or if the project may involve procedures that cannot be reasonably reviewed via the Expedited Review process, the protocol will be submitted for consideration at a Convened IRB meeting.

The Expedited Review process may be employed for new protocols, continuations of previously approved protocols, or amendments to approved protocols. To be eligible for approval via the Expedited Review process, a research activity must always meet both of the following conditions

(1) It must present no more than minimal risk to human participants; and
(2) It must involve only procedures listed in one or more of the categories of research activities listed below in Section 6A: Categories of Research Activities Eligible for Expedited Review. The IRB may use the expedited review procedure to review either or both of the following:

a. some or all of the research appearing in Section 6A below and found by the reviewer(s) to involve no more than minimal risk, and/ or
b. minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

When a protocol is reviewed by the expedited procedure process, reviewers are provided with and expected to review all information that the convened IRB would have received. For expedited review protocols, any IRB member can request to review the full protocol by contacting the IRB Office. The IRB Administrator will keep all IRB members advised of research that has been approved under expedited procedures by listing the research in the minutes of the next IRB meeting. Documentation for expedited reviews maintained in IRB records will include the category and circumstances that justify using expedited procedures.

I. Categories of Research Activities Eligible for Expedited Review

(1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met. (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.) (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

(2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows: (a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or (b) from other adults and children2, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

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

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;(e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

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

(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)

(8) Continuing review of research previously approved by the convened IRB as follows: (a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or (b) where no subjects have been enrolled and no additional risks have been identified; or (c) where the remaining research activities are limited to data analysis.

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

NOTE: the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review (expedited or convened) utilized by the IRB. Investigators must complete a Request for a Waiver of Consent And Waiver of Authorization under HIPAA (**Appendix H).** Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects. The categories in this list apply regardless of the age of subjects, except as noted. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. The expedited review procedure may not be used for classified research involving human subjects.

SECTION 8 - PROCEDURES FOR SUBMISSION TO THE CONVENED COMMITTEE INITIAL REVIEW OF RESEARCH

I. Categories of Research Activities that Require Review by the Convened IRB

Federal regulations, the Federal Policy (Common Rule) for the Protection of Human Subjects, and FDA regulations require that the IRB conduct review of research at convened meetings that does not meet the criteria of being exempt or expedited. The IRB Adminstrator and or the Director of the Lang Research Center will pre-review all submitted research and determine whether submitted research will be reviewed by the NYP/Q IRB or the designated IRB (WIRB). A convened meeting requires a Quorum unless the research falls into one or more of the categories appropriate for expedited review or the research is determined to be exempt from IRB review. In order to have their project reviewed by the convened IRB, Investigators must submit an Institutional Review Board Application for Initial and Expedited Review (**Appendix D**) and all documents outlined in the Checklist/Instructions for IRB Submissions (**Appendix E**), by the appropriate monthly deadline. Monthly submission deadlines are distributed to each department every January of the new year

- Initial applications that appear to involve more than minimal risk or that otherwise do not meet the criteria for Exemption from IRB review or Expedited Review;
- All other proposals that are determined by the IRB Administrator or an Expedited Reviewer to require Convened Committee Review; and
- Revisions to initial protocols that contain non-minor changes.

- Continuing Review of Projects that do not meet the requirement for Expedited Review

II. Procedures for Convened Committee's Review of Research

Keeping in mind the set deadlines for meeting submissions, Investigators who wish to conduct a research project involving human subjects shall submit: a completed Institutional Review Board Application for Initial and Expedited Review (**Appendix D**) and the following applicable items:

- Protocol - See Protocol Requirements/Template for IRB Submission **(Appendix G)** for required elements
- Protocol Lay Summary;
- Investigator's and all key personnel's Curriculum Vitae;
- Proposed Informed Consent Document(s)/Assent Form(s);
- Recruitment materials including ads, posters, radio commercials, etc
- Additional Subject materials, including all surveys and questionnaires, etc.
- Data Collection Forms
- Investigator Drug/Device Brochures
- Determination of Risk for Device Studies
- FDA 1572 form for Investigational New Drugs
- IND number for Investigational New Drugs (Either IND letter from the FDA or protocol that contains the IND number
- CITI Program for Human Subjects Protection for Investigator and all Key personnel.
- Financial Disclosure Form for Investigator and all Key personnel.
- Human Research Billing Analysis Form (**Appendix S**) must be forwarded to the Lang Research Center

After it has been determined that the research protocol application is complete, the IRB Administrator will submit the materials to the next monthly Convened Committee Meeting

The NYP/Q IRB meets at least once a month either in person or via telephone conference (as necessary). If the committee is required to conduct the meeting via telephone conference, all members must receive all pertinent material prior to the meeting and must be able to participate actively and equally in the discussions of the protocols. The committee will meet in person at least once a quarter.

1. The IRB Administrator will assign each protocol one primary (scientific) reviewer and one secondary (ICF)reviewer. The reviewers are always the IRB members with the applicable scientific and non-scientific expertise in the area of research. For studies that involve participants from vulnerable populations, one of the primary reviewers should have knowledge of or experience with that population. If one of the primary reviewers does not have such knowledge or experience, an appropriate consultant should be assigned. If an IRB member requires additional information to complete the review, that member may contact the IRB Office to make the request of the investigator.

2. If the Chair of the IRB determines that appropriate expertise for review is not available among the members of the IRB, the Chair may request that the Administrator seek a consultant from within or outside the NYP/Q community, or request that the research be reviewed by the designated IRB (WIRB).

3. The IRB Administrator will distribute to all IRB members the research protocol application materials in advance of an IRB meeting to allow for appropriate review. For members who are not the primary or secondary reviewer, IRB members attending the Convened meeting

will receive at least an abbreviated application package consisting of the protocol, recruitment materials, and consent forms 10 days before the IRB meeting. All members are expected to review and familiarize themselves with all protocols before the meeting.

4. The agenda packet will also contain the meeting agenda, the minutes from the last meeting (if available), and any other pertinent materials, including Continuing Review, Full Boards and Continuing Education. This meeting agenda will include a list of protocols that have been approved under the Expedited Review process since the last IRB meeting.

5. The primary reviewer shall complete the Primary Initial Review Checklist and the secondary reviewer will complete the Secondary Initial Review Checklist and be prepared to discuss their findings with the Convened IRB. If possible, the assigned reviewers will communicate any questions or concerns to the IRB Administrator so that the Protocol PI can be contacted for additional information before the meeting.

6. At the IRB meeting, the primary and secondary reviewers will provide a brief summary of each study, identify significant concerns, and report on the status (if available) of the Protocol PI's resolution of these concerns. All members are expected to discuss the significant concerns outlined by the primary and secondary reviewers, identify additional concerns, provide necessary clarifications, and/or propose solutions or modifications. The primary and secondary reviewer may make a recommendation on a vote. The IRB Administrator will keep minutes of the meeting, including key discussion points and IRB decisions.

III. Intervals for IRB Approval

Research activities are approved for a finite time period and use of any data after the approval period is considered unapproved research. The IRB will conduct Continuing Review of all ongoing research protocols at intervals relevant to the degree of risk involved, but not less than once per year. The purpose of the Continuing Review is to ensure the continuing protection of human participants in the research and the modification of the research, as appropriate, to reduce risk and incorporate any new knowledge that has been identified since the last Continuing Review.

Not less than once per year means that the research must be reviewed and approved on or before the one-year anniversary of the previous IRB review date (i.e. the date of expiration of the approval period), even though the research activity may not have been initiated until some time after the IRB granted approval. Under most conditions, it is assumed that the approval period will be 364 days from the date of initial IRB approval or 363 days when approval occurs in a leap year, unless the IRB determines at the time of initial review and approval that the degree of risk attendant to the protocol requires a shorter approval period. The approval period will be specified in the approval notice given to all Protocol PIs and no research can be conducted outside of the time period identified in the approval notice. For projects that have been approved with modifications, the effective date of the IRB's approvals starts on the date of the secondary (expedited review) approval.

SECTION 9 - PROCEDURES FOR CONTINUING REVIEW OF RESEARCH BY THE CONVENED IRB

The IRB is required to conduct substantive and meaningful continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. Continuing reviews will be

conducted by the convened IRB unless the research falls into one or more of the categories appropriate for expedited review. (See Section 6a)

Continuing Review of all ongoing research protocols is required to ensure that the protection of human participants is consistent throughout the execution of the research project and that the research protocol is revised, as appropriate, to include new knowledge generated since the last Continuing Review. Continuing Review shall not occur less frequently than once per year, but may occur more frequently depending upon the perceived risk of the research activity and the uniqueness of the specific research protocol.

Investigators are responsible for maintaining their IRB approval and for submitting a continuation application to the IRB. IRB approval is considered to have lapsed at midnight on the expiration date of the approval. As a courtesy, the IRB will send an email reminder to the Principal Investigator to remind them to submit their continuing review application and applicable documents. The reminder email is sent approximately 90 days before the expiration of the project. This reminder is designed as a courtesy to the Principal Investigator as investigators are responsible for maintaining their approval and for not conducting research outside of the review period. As an additional reminder, the deadline for Continuing Review Applications is indicated on all IRB correspondence to the Principal Investigator.

Neither the collection of prospective research data nor the performance of research-related procedures can occur after the expiration date of a project, unless the project has been resubmitted for review. Data collected after the previous approval date and before the approval of the continuation shall not be eligible for use in the research protocol. Continuing Review is required as long as the research project remains active for long-term follow-up of participants, even when the research is permanently closed to the enrollment of new participants and all participants have completed all research-related interventions.

Investigators must submit a Application for Continuing Review Form (**Appendix F**) on all active research protocols (i.e. research in progress and research in progress but closed to accrual) to the IRB, 3-months prior to the expiration date of IRB approval, along with the following information:

1. A copy of the most recent IRB approved protocol (required)
2. A copy of the last enrolled subject signed informed consent document (as applicable)
3. Copies of all translated informed consent documents being used in study (as applicable)
4. Copies of all subject materials-advertisements, surveys, questionnaires, etc(as applicable)
5. A Summary of any new findings or publications relevant to study (required)
6. A copy of the Request for a Waiver of consent And Waiver of Authorization Under HIPAA (Required if a consent/HIPAA waiver was requested)
7. A copy of any DSMB or Safety Reports (Required if applicable)
8. Indicate the addition or removal of any Investigators or Key Personnel and include the necessary documentation, such as a CV and the required CITI certificate.

The Application for Continuing Review Form (**Appendix F**) will require the following information: Summary of the protocol and status report of the research, to include (i) number of subjects accrued (ii) description of any adverse events or unanticipated problems involving risks to subject or others (iii) withdrawal of subjects from the research or complaints by subjects (iv) summary of recent literature related to the study (v) summary of any new information regarding risks to the subjects since the last review (vi) description of modifications to the research since the last review.

Upon receipt of the continuation application, the IRB Administrator will (1) make a preliminary review of the completeness of the materials or coordinate with the Protocol PI to achieve completion; (2)

review the application to determine whether the Expedited or Convened Committee Review process is appropriate; and (3) enter selected information from the Continuing Approval Request form into the IRB Manager database.

In conducting continuing review of research ineligible for expedited review, all IRB members are provided with and review all of the above-referenced material. The process of reviewing Continuing Review is similar to the process of reviewing a new project. A Primary Reviewer will be assigned to review and report on all applicable materials, as noted above. At the convened IRB Board meeting, the Primary Reviewer will lead the IRB through the completion of the regulatory criteria for approval, including the informed consent document, in the Continuing Reviewer's Checklist.

I. Categories of Research Activities that Require Continuing Review by the Convened IRB:

1. the research is continuing to enroll new subjects;
2. the research project remains active for long-term follow-up of participants, even when the research is permanently closed to the enrollment of new participants and all participants have completed all research-related interventions;
3. the remaining research activities are limited to analysis of private identifiable information.

II. Procedures for Convened Committee's Continuing Review of Research

The NYP/Q IRB meets at least once a month either in person or via telephone conference (as necessary). If the committee is required to conduct the meeting via telephone conference, all members must receive all pertinent material prior to the meeting and must be able to participate actively and equally in the discussions of the protocols. The committee will meet in person at least once a quarter.

The IRB Administrator will assign each continuing review one primary (scientific) reviewer. The reviewers are always the IRB members with the applicable scientific and non-scientific expertise in the area of research. For studies that involve participants from vulnerable populations, one of the primary reviewers should have knowledge of or experience with that population. If one of the primary reviewers does not have such knowledge or experience, an appropriate consultant should be assigned. If an IRB member requires additional information to complete the review, that member may contact the investigator directly or may contact the IRB Office to make the request of the investigator. Protocol reviewers may use the Continuing Reviewer's Checklist as a guide to completing their review.

If the Chair of the IRB Administrator determines that appropriate expertise for the continuing review is not available among the members of the IRB, the Chair may request that the Administrator seek a consultant from within or outside the NYP/Q community

The IRB Administrator will distribute to all IRB members the research protocol continuing review application materials in advance of an IRB meeting to allow for appropriate review. For protocols for which they are not primary reviewers, IRB members attending the Convened meeting will receive at least an abbreviated continuing review application package consisting of the protocol, recruitment materials, and consent forms 10 days before the IRB meeting. All members are expected to review and familiarize themselves with all protocols before the meeting.

The primary reviewer shall complete the Continuing Reviewer's Checklist and be prepared to discuss their findings with the Convened IRB. If possible, the assigned reviewers will

communicate any questions or concerns to the IRB Administrator so that the Protocol PI can be contacted for additional information before the meeting.

At the IRB meeting, the primary reviewer will provide a brief summary of each study, identify significant concerns, any comments on the informed consent, adverse events, subject enrollments, amendments, etc., and report on the status (if available) of the Protocol PI's resolution of these concerns. All members are expected to discuss the significant concerns outlined by the primary reviewer, identify additional concerns, provide necessary clarifications, and/or propose solutions or modifications, if applicable. The primary reviewer may make a recommendation on a vote. The IRB Administrator will keep minutes of the meeting, including key discussion points and IRB decisions.

Determinations for review of Continuing Review are the same as Section 5B:. Possible Outcomes from an IRB Review and follows the same as Section 7C: Intervals for IRB Approval.

III. Categories of Continuing Review Eligible for Expedited Review.

The following types of protocols will receive Continuing Review under the Expedited process:

1. a protocol that falls within one of the seven categories of research activities eligible for Expedited Review set forth above in Section: Categories of Research Activities Eligible for Expedited Review.

2. a protocol that was initially reviewed and approved under the Expedited process and to which no major changes have been made necessary for Convened Committee Review; OR

3. a protocol that was reviewed and approved previously under the Convened Committee process, but meets the following conditions:
   a. the research is permanently closed to the enrollment of new subjects; (ii) all participants have completed all research-related interventions; *and* (iii) the research remains active only for long-term follow up of subjects; *OR*
   b. no subjects have been enrolled and no additional risks have been identified; *OR*
   c. the remaining research activities are limited to data analysis. *OR*

4. research, not conducted under an investigational new drug application or investigational device exemption, where categories 2 through 7 in Section 6: Categories of Research Activities Eligible for Expedited Review and item (3) above does 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.

Continuing Review That Does Not Meet Section 6: Categories of Research Activities Eligible for Expedited Review
Any protocol which poses or has been revised to pose more than minimal risk will be reviewed under the Convened Committee process. And, generally, protocols that initially required Convened Committee Review will receive Continuing Review under the same process.

The IRB Administrator will attempt to assign continuation applications to the protocol's original Expedited Reviewer or primary reviewers. The Continuing Reviews for the Convened IRB will be added to a future meeting agenda, and every member of the IRB will receive the continuation package.

IV. Failure to Submit Research Protocol for Continuing Review:

IRB approval is considered to have lapsed at midnight on the expiration date of the approval. If IRB approval of a specific study expires before continuing review and approval occur, investigators must stop all research activities involving human subjects related to that study (45 CFR 46.103(b)), except where they judge that it is in the best interests of already enrolled subjects to continue to participate. When investigators make this judgment, they must promptly notify the IRB (45 CFR 46.103(b)(5)). When the IRB reviews the investigator's decision, it may decide whether it is in the best interests of already enrolled subjects to continue to participate in the research by considering the best interests of subjects either one at a time or as a group. If an IRB determines that it is not in the best interests of already enrolled subjects to continue to participate, investigators must stop all human subjects research activities, including intervening or interacting with subjects, or obtaining or analyzing identifiable private information about human subjects (45 CFR 46.103(b)).

The Investigators must plan ahead in order to meet required continuing review dates. Study expiration can occur even if the investigator has provided the continuing information before the expiration date because of meeting deadlines vs. submission dates. Therefore, investigators must allow sufficient time (3 months) for IRB review before the expiration date.

An expiration letter will be sent to investigators by the last date of the approval period (To Apply for Reinstatement of Project; See Section 8E)

Failure to submit continuing review information on time is considered non-compliance and will be handled accordingly

- If the study is FDA-regulated, the IRB Chair must follow FDA requirements set forth in 21 CFR 56.108(b)(3), which is notification to the FDA that the study has been allowed to lapse.
- The sponsoring agency, private sponsor, or other federal agencies must be informed of any lapse in research as appropriate.
- Once suspended, IRB review and re-approval must occur prior to re-initiation of the research.

V. Steps for Applying for Reinstatement of Expired Project:

The IRB will allow a project to possibly be reinstated If the Investigator submits the appropriate documentation within 30 days. If the Investigator fails to meet the 30 day deadline, the project will be deemed terminated. Once a project is terminated, the Investigator must submit the project as new.

An Investigator who meets the 30 day deadline and wishes to apply for re-instatement of their project, must do the following:

- Submit appropriate Continuing Review Documentation
- Submit documentation of any research activity that occurred without IRB approval
- Submit any Protocol Deviations that occurred while study was expired.
- Submit documentation to the IRB outlining the reasons the project was allowed to expire and include steps that will be taken to insure that the oversight will not occur again

NO research activity may occur while waiting for the IRB's decision regarding an expired project

VI. Independent Verification From Sources Other than the Investigator of Any Information Regarding the Study Including That No Material Changes Have Occurred Since the Previous IRB Review

Protecting the rights and welfare of subjects sometimes requires that the IRB verify independently, utilizing sources other than the investigator, information about various aspects of the study including but not limited to adverse event reporting, information in the scientific literature, reports of drug toxicity, drug approval status, and that no material changes occurred during the IRB-designated approval period. The IRB will consider the following factors in determining which studies require such independent verification: (i) The probability and magnitude of anticipated risks to subjects. (ii) The likely medical condition of the proposed subjects. (iii) The probable nature and frequency of changes that may ordinarily be expected in the type of research proposed. (iv) Prior experience with the Investigator and research team. (v) Any other factors that the IRB deems relevant. In making determinations about independent verification, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period, may retrospectively require such verification at the time of continuing review or may require such verification at any time during the approval period in the light of new information.

SECTION 10 – INFORMED CONSENT PROCESS

Federal regulations at 45 CFR 46.116 state "no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the 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. The exceptions to this requirement are limited and must be approved by the IRB before the commencement of the study. While there are a few circumstances in which the IRB may grant a waiver or provide for an alternative to the informed consent process, the principle of obtaining legally effective informed consent is the standard for all research with human participants.

Informed Consent is an ongoing process for both the Protocol PI and the participant. It is the process by which the research study is explained to the potential participant, who is then encouraged to asks questions and have an open discussion with the Protocol PI. The process involves the ongoing, interactive exchange of information, beginning with the recruitment of the participant and ending with the completion of the study. The basic elements of this process are: full disclosure of the nature of the research and the participant's involvement; adequate comprehension on the participant's part; minimization of the possibility of coercion or undue influence; and the participant's voluntary choice to participate.

The IRB has the final authority as to the content of the consent form presented to the prospective study participants. The IRB may require that the form include, in addition to the information required by the regulations and/or the Sponsor, information dictated by the IRB, as voted by the majority of members.

I. The Process of IRB Review of Informed Consent Documents

Upon submission of a project to the IRB, the IRB Administrator will make the initial determination of whether it qualifies for Expedited Review or the Convened Committee Review Process, the Expedited Reviewer or the Primary Reviewer will review the consent documents for content and form and either approve them or recommend changes. The IRB is responsible for determining whether waivers of informed consent or documentation of informed consent are applicable and appropriate.

In the case of Convened Committee Review, the IRB members at the convened meeting will review the consent process (or request for waiver of consent) and the content and form of the consent documents. The IRB will either approve the consent documents or recommend changes to their content or to some other aspect of the consent process. In the event the consent process/documents are in a language other than English, the IRB must receive appropriately translated documents and assess their accuracy before approving their use.

If the Expedited Reviewer or the Primary Reviewer request changes, the IRB Administrator will inform the Protocol PI in writing of the required changes. When IRB-requested changes are returned by the Protocol PI, the IRB Administrator will confirm that all the changes have been made and present the revised informed consent to the Expedited Reviewer or Primary Reviewer for review and approval or place them on the agenda of the next available meeting of the convened IRB.

The IRB Administrator will document in the minutes, the outcome of any IRB discussion relating to the consent process or documents, including but not limited to:

- Use of non-English documents (See Section)
- Use of a translator (See Section)
- Use of consent from a legally authorized representative
- Consent requirements relating to participants from vulnerable populations
- Waiver of consent
- Waiver of documentation of consent
- Any directed changes by the IRB.

Once consent documents are approved by the IRB, The IRB Administrator will issue an approval and expiration date established for the protocol by the IRB. These IRB-approved versions must be used during the consent process, as they are the only versions considered valid. The protocol approval period expires at midnight on the date of expiration and therefore, the consent form expires then as well. The dates of approval and expiration are stamped on all consents and also provided to the Protocol PI on all IRB correspondence. All enrolled subjects must sign a NYP/Q IRB or designated IRB (WIRB) stamped consent.

The consent form, which has been approved by the NYP/Q IRB or other designated IRB, is to be presented to the potential research subject, is to be signed by the subject and is to be properly witnessed by an impartial observer, all in a manner approved by the NYP/Q /IRB guidelines. The consent form shall be kept as a matter of record. When appropriate, time will be allowed to elapse between the explanation of the study and disclosure of risks, and the signing of the consent form, to permit due consideration by the subject. The consent form shall contain no exculpatory language through which the subject is made to waive, or appear to waive, any of his/her legal rights, or to release the institution from liability for negligence. If the subject is under 18 years of age or otherwise legally incompetent, the consent of the parent(s) or legally authorized representative must be procured. Signed written consent is mandatory

unless the IRB specifically determines that oral consent or other procedure is acceptable, or waives the requirement for consent.

II. Required Elements of Informed Consent Documents

Before a human subject participates in an investigation informed consent must be obtained from the subject. The following basic elements of informed consent, as required under 21 CFR 50.25(a)-(b) and 45 CFR46.116-117, must be included in every document.

1. a statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;
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 which 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 that notes the possibility that the Food & Drug Administration may inspect the records;
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; and
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. It is particularly important for subjects and prospective subjects to understand and have complete confidence that declining to participate in research will not compromise their care.

The regulations also recommend that, when appropriate, one or more of the following elements of information should also be provided to each subject:

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) which are currently unforeseeable;
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject'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 which may relate to the subject's willingness to continue participation will be provided to the subject; and
6. The approximate number of subjects involved in the study.

A. Compensation for Injury

The IRB will ensure that subjects are provided with accurate information about the availability of compensation and/or treatment for injury occurring in the research that it reviews. “Injury” may include physical injury, psychological harm, social harm, or harm to

one's dignity, depending upon the nature of the research. Investigators at NYP/Q have an obligation to make every effort to prevent study-related injuries and illnesses. Emergency care will be provided if a subject is injured or becomes ill while participating in research. The costs of emergency care will be charged to the subject or the subject's health insurer. No funds are available from NYP/Q, NYP/Q's affiliates, the State of New York, or the Federal government to compensate subjects for a study-related injury or illness. The extent to which and conditions under which a corporate sponsor of research (e.g., a company-sponsored clinical trial) will pay the costs of emergency or ongoing care of study-related injuries must be clearly described in the informed consent document and explained during the informed consent process.

Therefore, NYP/Q/IRB requires the following statement be included in all consent forms:

"In the event of a research related question or injury, you should notify (list Doctor(s) name and phone number). Neither the New York Presbyterian/Queens, nor any of its staff or agents, will provide any form of compensation to you if you sustain an injury as a result of research. However, this does not waive any of your rights.

For information concerning your rights as a research participant, you should contact the Institutional Review Board (IRB) at The New York Presbyterian/ Queens whose office telephone number is 718-670-1194"

B. Payment to Research Subjects

The IRB will review any proposed payments to research subjects associated with the research that they oversee. Payments to research subjects may not be of such an amount as to result in coercion or undue influence on the subject's decision to participate. Payments may not be provided to subjects on a schedule that results in coercion or undue influence on the subject's decision to continue participation.

III. Consent Monitoring

In reviewing the adequacy of informed consent procedures for proposed research, the IRB may on occasion determine that special monitoring of the consent process by an impartial observer (consent monitor) is required in order to reduce the possibility of coercion and undue influence. Such monitoring may be particularly warranted where the research presents significant risks to subjects, or if subjects are likely to have difficulty understanding the information to be provided. Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with a particular investigator or a research project. The IRB may also require that investigators include a "waiting period" within the consent process, or employ devices such as audiovisual aids or tests of comprehension.

IV. NYP/Q IRB Template Consent Forms

The NYP/Q IRB Administrator may provide the Protocol PI with Template Consent Form (**Appendix P**) when the PI is required to draft one. The Protocol PI should keep in mind that the consent form must be written in language understandable to the participant, preferably at the 8th grade level. The use of a readability index is recommended to help prepare consent forms that are easy to read.

The NYP/Q Template consent Forms also contain language that is required in all Informed Consent Documents for Investigator Initiated Protocols. The template consent forms contain all the required elements of consent, as outlined in Section 9A.

OHRP guidance provides the following tips when writing an informed consent:

The process of obtaining informed consent must comply with the requirements of 45 CFR 46.116. The documentation of informed consent must comply with 45 CFR 46.117. The following comments may help in the development of an approach and proposed language by investigators for obtaining consent and its approval by IRBs:

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

- Use of the first person (e.g., "I understand that ...") can be interpreted as suggestive, may be relied upon as a substitute for sufficient factual information, and can constitute coercive influence over a subject. Use of scientific jargon and legalese is not appropriate. Think of the document primarily as a teaching tool not as a legal instrument.

- Describe the overall experience that will be encountered. Explain the research activity, how it is experimental (e.g., a new drug, extra tests, separate research records, or nonstandard means of management, such as flipping a coin for random assignment or other design issues). Inform the human subjects of the reasonably foreseeable harms, discomforts, inconvenience and risks that are associated with the research activity. If additional risks are identified during the course of the research, the consent process and documentation will require revisions to inform subjects as they are re-contacted or newly contacted.

- Describe the benefits that subjects may reasonably expect to encounter. There may be none other than a sense of helping the public at large. If payment is given to defray the incurred expense for participation, it must not be coercive in amount or method of distribution.

- Describe any alternatives to participating in the research project. For example, in drug studies the medication(s) may be available through their family doctor or clinic without the need to volunteer for the research activity.

- The regulations insist that the subjects be told the extent to which their personally identifiable private information will be held in confidence. For example, some studies require disclosure of information to other parties. Some studies inherently are in need of a Certificate of Confidentiality which protects the investigator from involuntary release (e.g., subpoena) of the names or other identifying characteristics of research subjects. The IRB will determine the level of adequate requirements for confidentiality in light of its mandate

to ensure minimization of risk and determination that the residual risks warrant involvement of subjects.

- If research-related injury (i.e. physical, psychological, social, financial, or otherwise) is possible in research that is more than minimal risk (see 45 CFR 46.102[g]), an explanation must be given of whatever voluntary compensation and treatment will be provided. Note that the regulations do not limit injury to "physical injury". This is a common misinterpretation.

- The regulations prohibit waiving or appearing to waive any legal rights of subjects. Therefore, for example, consent language must be carefully selected that deals with what the institution is voluntarily willing to do under circumstances, such as providing for compensation beyond the provision of immediate or therapeutic intervention in response to a research-related injury. In short, subjects should not be given the impression that they have agreed to and are without recourse to seek satisfaction beyond the institution's voluntarily chosen limits.

- The regulations provide for the identification of contact persons who would be knowledgeable to answer questions of subjects about the research, rights as a research subject, and research-related injuries. These three areas must be explicitly stated and addressed in the consent process and documentation. Furthermore, a single person is not likely to be appropriate to answer questions in all areas. This is because of potential conflicts of interest or the appearance of such. Questions about the research are frequently best answered by the investigator(s). However, questions about the rights of research subjects or research-related injuries (where applicable) may best be referred to those not on the research team. These questions could be addressed to the IRB, an ombudsman, an ethics committee, or other informed administrative body. Therefore, each consent document can be expected to have at least two names with local telephone numbers for contacts to answer questions in these specified areas.

- The statement regarding voluntary participation and the right to withdraw at any time can be taken almost verbatim from the regulations (45 CFR 46.116[a][8]). It is important not to overlook the need to point out that no penalty or loss of benefits will occur as a result of both not participating or withdrawing at any time. It is equally important to alert potential subjects to any foreseeable consequences to them should they unilaterally withdraw while dependent on some intervention to maintain normal function.

- Don't forget to ensure provision for appropriate additional requirements which concern consent. Some of these requirements can be found in sections 46.116(b), 46.205(a)(2), 46.207(b), 46.208(b), 46.209(d), 46.305(a)(5-6), 46.408(c), and 46.409(b). The IRB may impose additional requirements that are not specifically listed in the regulations to ensure that adequate information is presented in accordance with institutional policy and local law.

V. Implementing the Most Current, IRB-Approved Consent Form

Every IRB approved consent document will contain the NYP/Q IRB or the designated IRB (WIRB) stamp, which states the assigned IRB number and the date of approval and date of expiration. The final approved consent form must contain the date of approval and date of expiration If a revision to the consent form is approved by the IRB before the expiration of the

previous version, the Protocol PI must ensure that participants are signing the most current, IRB approved consent form

VI. Consent Form Revisions

When changes are necessary for the current IRB-Approved Consent Form, due to amendments, addendums, administrative changes, etc., these changes must be submitted and approved by the IRB before an participants can sign the new version. Along with applicable documentation, the IRB must receive a Request for IRB Review Form (**Appendix L**), a copy of the redlined (tracked changes) consent form and a "clean' copy of the consent form. Changes that are considered administrative, such as .grammatical corrections, address/phone number changes, New PI, etc. may be processed and approved by the IRB Administrator.

VII. Re-Consenting Participants

The Protocol PI has a responsibility to inform research participants of any new information that might affect a participant's willingness to continue participating in the research. While some new information may require re-consenting all participants with a revised consent form or addendum (e.g., discovery of a previously unknown serious side effect), other changes may require only notification to active participants (e.g., grammatical corrections, minor changes not affecting the risk/benefit ratio). The timeliness and method of informing participants and the necessity of re-consenting will depend on the seriousness of the new information and will be decided and communicated to the Protocol PI when the IRB approves the revisions.
In cases where participants have completed active study or follow-up procedures and new safety information is discovered that may affect a participant's further participation or longterm risks from the treatment, the participant must be informed of this new information.

VIII. Waiver or Alteration of Informed Consent Requirements: Minimal Risk Research

Federal regulations at 45 CFR 46.116(d) permit an IRB to approve a consent procedure that eliminates or alters the required elements of informed consent, or to waive the requirement to obtain informed consent altogether. If a Protocol PI wishes to receive a waiver of Consent, they must complete and submit the Request for a Waiver of Consent And Waiver of Authorization under HIPAA (**Appendix H**)In order to approve such a waiver or alteration, the IRB must find and document that: (i) The research involves no more than minimal risk to the subjects. (ii) The waiver or alteration will not adversely affect the rights and welfare of the subjects. (iii) The research could not practically be carried out without the waiver or alteration. (iv) Whenever appropriate, the subjects will be provided with additional pertinent information after participation. These findings and their justifications will be clearly documented in IRB minutes.

Federal regulations at 45 CFR 46.117(c) permit an IRB to waive the requirement to obtain written documentation of informed consent. In order to approve such a waiver, the IRB must find and document either of the following conditions: (i) The only record linking the subject and the research would be the consent document and the principle risk would be potential harm resulting from a breach of confidentiality. In this case, each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or (ii) The research presents no more than minimal risk of harm to subjects and involves procedures or activities for which written consent is not normally required outside of the research context. In cases in which the documentation requirement is waived, the IRB may require the Responsible Investigator to provide subjects with a written statement regarding the research. These findings and their justifications will be clearly documented in IRB minutes.

This waiver provision is not applicable to research governed by FDA regulations and will not approve such alterations or waivers for FDA-regulated research.

IX. Use of a Surrogate Consent

Informed consent must be obtained from all participants who are mentally capable of providing their effective informed consent to participate in the proposed research. Protocol PI's with studies that allow/request the use of a Surrogate Consent must indicate such on the IRB application and the request will be voted on by the Convened IRB. All informed consents must reflect the IRB's approval of a Surrogate Consent with the proper signature lines. No study may enroll subjects through the use of a Surrogate Consent without prior IRB approval. Additionally, any study that does not have approval to obtain a Surrogate Consent must provide the IRB with a Consent Document that does not contain signature lines for such.

For studies that allow/request the use of a Surrogate Consent for participants who are incapable of providing effective informed consent due to some cognitive or decisional impairment, there are two ways in which their participation may be allowed:

1. A Health Care Proxy may consent to enroll a participant in any research protocol that has been approved by the IRB.

2. If there is no health care proxy, a legally acceptable representative may permit the participant's enrollment in IRB-approved research if (a) the risk is minimal, regardless of whether the participant would derive any benefit; OR (b) the risk is greater than minimal, but the research potentially carries a direct benefit to the participant.

A legally acceptable representative is to be chosen in the order of priority listed determined as followed:

1. The spouse;
2. A son or daughter eighteen years of age or older;
3. A parent;
4. A brother or sister eighteen years of age or older;
5. A close friend.

Additionally, the following criteria must be met in order for the NYP/Q IRB to approve the use of a Health Care Proxy/Legally Acceptable Representative:

1. There is potential benefit over standard treatment;
2. Standard treatment has not being withheld;
3. Enrollment in the study is in the best interest of the patient; and
4. Participation in the research would not be contrary to the known wishes of the patient

Finally, the research subject must be given the opportunity to consent or decline participation if their cognitive or decisional impairment is reversed.

If neither a legal representative nor a family member is available, then a participant may not be enrolled in any research protocol.

X. Obtaining Consent from Non-English Speakers

Department of Health and Human Services regulations for the protection of human subjects require that informed consent information be presented "in language understandable to the subject" and, in most situations, that informed consent be documented in writing (45 CFR

§46.116 and §46.117). Where informed consent is documented in accordance with §46.117(b)(1), the written consent document should embody, in language understandable to the subject, all the elements necessary for legally effective informed consent. Subjects who do not speak English should be presented with a consent document written in a language understandable to them. OPRR strongly encourages the use of this procedure whenever possible. Alternatively, §46.117(b)(2) permits oral presentation of informed consent information in conjunction with a Short Form Written Consent (**Appendix N**)document (stating that the elements of consent have been presented orally) and a written summary of what is presented orally. A witness to the oral presentation is required, and the subject must be given copies of the short form document and the summary. When this procedure is used with subjects who do not speak English, (i) the oral presentation and the short form written document (see sample below) should be in a language understandable to the subject; (ii) the IRB-approved English language informed consent document may serve as the summary; and (iii) the witness should be fluent in both English and the language of the subject. At the time of consent, (i) the short form document should be signed by the subject (or the subject's legally authorized representative); (ii) the summary (i.e., the English language informed consent document) should be signed by the person obtaining consent as authorized under the protocol; and (iii) the short form document and the summary should be signed by the witness. When the person obtaining consent is assisted by a translator, the translator may serve as the witness.

Whether a full-length or a Short Form Written Consent (**Appendix N**) is utilized the IRB must received all foreign language versions of the documents as a condition of approval. Expedited review of these versions is acceptable if the Investigators must obtain the legally effective informed consent of the prospective subject, or the subject's legally authorized representative, before the subject can be included in research or before investigators can perform any research-related procedures, unless the IRB formally and specifically waives this requirement.

XI. Oral Informed Consent for Non-English Speakers

Oral consent is the process of obtaining consent without the use of a written document. The IRB may approve the use of oral consent where the participant is (1) blind, (2) illiterate, or (3) unable to write his or her name or (4) otherwise approved by the IRB.

A. Oral consent must be documented.
The Protocol PI should provide to the IRB for review and approval the following documentation: (a) a written summary or script from the Protocol PI of what is to be said to the participant or his or her legally authorized representative, and (b) an information sheet documenting that the elements of informed consent required by federal regulations and the IRB have been presented orally to the participant or the participant's legally authorized representative. The information sheet should be signed by (a) the person obtaining consent; and (b) a witness to the oral presentation, when appropriate, as determined by the IRB. A copy of the information sheet shall be provided to the participant or the representative, when possible. 2. The IRB may also decide that oral consent be documented, instead or additionally, by another method such as audio or video-recording.

XII. Translations of Informed Consent Documents for Non-English Speakers

The IRB must approve all foreign language versions of written or oral consent documents and all survey instruments as a condition of approval under 45 CFR 46.117(b)(2).

The Protocol PI **must** first obtain and receive the current IRB-approved consent before beginning the translation process. Upon receipt of the current IRB-approved consent form, the Protocol PI may then choose one of the following translation processes:

1. Submit a copy of the current IRB approved English consent form for translation service**.** After receiving the appropriate translations, the Protocol PI must submit the translated consent form along with the Certificate of Authenticity to the IRB, along with a Request for IRB Review Form (**Appendix L**),
2. Submit a copy of the current IRB approved English consent form to the Protocol Sponsor for translation services. After receiving the appropriate translations, the Protocol PI must submit the translated consent form along with the Certificate of Authenticity to the IRB, along with a Request for IRB Review Form (**Appendix L**).

The IRB Administrator may Administratively approve translated consent form that are submitted with a Certificate of Authenticity.

XII. Obtaining Oral Consent from Non-English Speakers

Where oral consent is allowable, as defined in Section9h, a translator fluent in both English and the participant's language should translate the IRB-approved English consent form orally to the participant in front of a witness. The IRB may require that the translator be a non-research team member. The translator may serve also as the witness.

XIII. Questionnaires for Non-English Speakers

A. *Written Questionnaires*: When participants who do not understand English are involved in studies that require answering questionnaires, the questionnaires must be translated into a language that those participants understand, while maintaining the same format. Furthermore, the translated questionnaires must convey the same meaning as the original English versions. Otherwise, the responses of non-English speakers will not be comparable to those of English speakers. The translation process shall be the same as described in Section 10XI.

B. *Verbal Questionnaires*: Verbally-administered questionnaires shall be the same for English and non-English speakers in both content and format. The Protocol PI may select one of these two translation options: (1) Verbal Administration: The questionnaire does not require a written translation. Instead, it will be verbally administered by a person who is fluent in both languages. (2) Written Translation: The questionnaire will be translated into a language understandable to the participant as described in Section 9i.The translated questionnaire must be administered verbally by a person who is fluent in the participant's language, but this person need not be fluent in English.

XIV. Other Documents for Non-English Speakers

If the research involves the use of oral scripts, educational materials, advertisements, or other documents in addition to the consent forms and questionnaires, the Protocol PI must describe in the protocol the measures that will be taken by the research team to ensure that the information contained in those documents will be conveyed to the participants in an understandable way. Under normal conditions, translated copies should be submitted to the IRB for review and approval. The extensive use of a translator to work with the research participant in order to communicate the information in the materials is an acceptable alternative to providing translated documents.

Note: Section 10XI. applies to obtaining Oral Consent from all subjects, when approved by the IRB.

XVII. Genetic Research and Informed Consent

Genetic testing using proven methods for clinical purposes does not represent research. Genetic testing that is done for the acquisition of generalizable new knowledge constitutes research and all such studies that include genetic testing must conform to Federal, State and Local regulations for research in human subjects.

As described in the section on Genetic Testing in the OHRP Guide Book, the examination of biological samples (tissue, blood and other body fluids) in general represents no direct physical harm to subjects (inflicts no physical pain or suffering). However, genetic testing carries with it the very real possibility of psychosocial risks to the subjects (the risk of harm from learning genetic information about oneself, social stigmatization, discrimination, labeling, and potential loss of, or difficulty in, obtaining employment or insurance). Genetic studies that generate information about subjects' personal health risks can provoke anxiety and confusion and damage familial relationships. Information obtained through genetic research may also have serious repercussions for the subject's family members. Consequently, these studies should not be considered to present no risk or minimal risk. Thus, if a biological sample can be linked back to a subject, directly or indirectly, that research will require full board review at a convened meeting of the IRB.

A. Disclosure of Results of Genetic Tests

The IRB requires that the consent document contain a statement included in the description of the study that indicates whether or not the information that derives from genetic studies will be given to that subject. NY law prevents disclosure of test results unless they are approved tests performed in a certified lab.

The IRB has determined the following language is acceptable:

> "There is a chance of discrimination if the results of the testing show a genetic disorder. You might be denied a job or promotion, or denied health or life insurance if employers or insurance companies find out. You may experience other forms of discrimination. We will not release any information to anyone without your written permission. However, it is possible that genetic information may be gotten through legal means and then affect your ability to get insurance or a job. In cases where parents and children are both tested, tests may reveal the possibility that the father is not the biological parent (if applicable)."

XVIII. Certificates of Confidentiality

Where research involves the collection of highly sensitive information about individually identifiable subjects, the IRB may determine that special protections are needed to protect subjects from the risks of investigative or judicial processes. In such situations, the IRB may require that an investigator obtain a DHHS Certificate of Confidentiality (C of C). The C of C protects against the involuntary release of sensitive information about individual subjects for use in Federal, State, or local civil, criminal, administrative, legislative, or other legal proceedings. The C of C does not prohibit voluntary disclosure of information by an investigator, such as voluntary reporting to local authorities of child abuse or of a communicable disease. In addition, the C of C does not protect against the release of information to DHHS or FDA for audit purposes. Consequently, it is important for investigators to identify beforehand all conditions under which they will voluntarily release information to third parties. the IRB will require that these conditions for release be stated clearly and explicitly in the informed consent document.

XIX. Assent of Children- See Section 14

SECTION 11 – RECRUITMENT OF SUBJECTS

FDA requires that an Institutional Review Board (IRB) review and have authority to approve, require modifications in, or disapprove all research activities covered by the IRB regulations [21 CFR 56.109(a)]. An IRB is required to ensure that appropriate safeguards exist to protect the rights and welfare of research subjects [21 CFR 56.107(a) and 56.111]. In fulfilling these responsibilities, an IRB is expected to review all the research documents and activities that bear directly on the rights and welfare of the subjects of proposed research. The protocol, the consent document and, for studies conducted under the Investigational New Drug (IND) regulations, the investigator's brochure are examples of documents that the IRB should review. The IRB should also review the methods and material that investigators propose to use to recruit subjects.

Direct advertising for research subjects, i.e., advertising that is intended to be seen or heard by prospective subjects to solicit their participation in a study, is not in and of itself, an objectionable practice. Direct advertising includes, but is not necessarily limited to: newspaper, radio, TV, bulletin boards, posters, and flyers that are intended for prospective subjects. Not included are: (1) communications intended to be seen or heard by health professionals, such as "dear doctor" letters and doctor-to-doctor letters (even when soliciting for study subjects), (2) news stories and (3) publicity intended for other audiences, such as financial page advertisements directed toward prospective investors.

I. Recruitment Guidelines

No claims should be made, either explicitly or implicitly, that the drug, biologic or device is safe or effective for the purposes under investigation, or that the test article is known to be equivalent or superior to any other drug, biologic or device. Such representation would not only be misleading to subjects but would also be a violation of the Agency's regulations concerning the promotion of investigational drugs [21 CFR 312.7(a)] and of investigational devices [21 CFR 812.7(d)].

Advertising for recruitment into investigational drug, biologic or device studies should not use terms such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational. A phrase such as "receive new treatments" leads study subjects to believe they will be receiving newly improved products of proven worth.

Advertisements should not promise "free medical treatment," when the intent is only to say subjects will not be charged for taking part in the investigation. Advertisements may state that subjects will be paid, but should not emphasize the payment or the amount to be paid, by such means as larger or bold type.

Generally, FDA believes that any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest. When appropriately worded, the following items may be included in advertisements. It should be noted, however, that FDA does not require inclusion of all of the listed items.

1. The name and address of the clinical investigator and/or research facility;
2. The condition under study and/or the purpose of the research;
3. In summary form, the criteria that will be used to determine eligibility for the study;
4. A brief list of participation benefits, if any (e.g., a no-cost health examination);
5. The time or other commitment required of the subjects; and
6. The location of the research and the person or office to contact for further information.

II. Advertisements and Recruitment Incentives

The IRB is required to review and approve all advertisements (including posters, announcements, radio ads, notices, displays, etc.) and recruitment incentives associated with the research that they oversee. Approval of the IRB must be obtained prior to the use of any advertisement or recruitment incentive. Advertisements and incentives are directly related to the informed consent process and must be consistent with prohibitions on coercion and undue influence. Any change in an approved advertisement or recruitment incentive must be approved by the IRB prior to being put into effect. The IRB may require that advertisements and recruitment incentives for proposed research be modified to minimize the possibility of ambiguity, coercion or undue influence.

III. IRB Review and Determinations of Advertisement and Recruitment

When direct advertising is to be used, the IRB should review the information contained in the advertisement and the mode of its communication, to determine that the procedure for recruiting subjects is not coercive and does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol. The IRB should review the final copy of printed advertisements to evaluate the relative size of type used and other visual effects. When advertisements are to be taped for broadcast, the IRB should review the final audio/video tape. The IRB may review and approve the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording. The review of the final taped message prepared from IRB-approved text may be accomplished through expedited procedures. The IRB may wish to caution the clinical investigators to obtain IRB approval of message text prior to taping, in order to avoid re-taping because of inappropriate wording.

No participant may be recruited using material that has not been seen by the IRB. The Protocol PI may either submit recruitment material at the time of an Initial Submissions or by using the Request for IRB Review Form (**Appendix L**). The materials will be reviewed by with the Convened Committee or through Expedited Review. The Protocol PI will receive a letter from the IRB Administrator outlining the IRB's determination of any advertising. Approval letters will include a listing of the approved documents, which will either contain the Sponsor Version of the documents or the NYP/Q IRB stamp dated approval. Any amendments to approved advertising must be resubmitted to the IRB using the Request for IRB Review Form (**Appendix L**)

SECTION I2 – AMENDMENTS TO PREVIOUSLY APPROVED RESEARCH

No changes in approved research (including all study procedures, subject recruitment materials, advertisements and informed consent documents and procedures) may be initiated without prior IRB approval, except where necessary to eliminate apparent immediate hazards to subjects. No research may be continued beyond the IRB-designated approval period. All modifications, amendments or changes to the approved use of a drug, diagnostic test or device, must be submitted to the IRB, along with a completed, Request for IRB Review Form (**Appendix L**), submit it in a timely manner and obtain approval of the IRB before initiation of the modification. The Principal Investigator or Sponsor must submit all amendments to a previously approved project to the IRB for review

Definitions of Modifications and IRB Review Requirements:

- Minor modifications must meet all the following criteria:
    - Involve the addition of no more than minimal risk, or
    - Reduce a risk that reviewed and approved previously by the convened IRB
    - Involve the addition of procedures that would be exempt from IRB review or eligible for review under the Expedited Review process.

Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories found under Expedited Review (found in Section 7), may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects= financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

The expedited review procedure may not be used for classified research involving human subjects. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.

Any modification that does not meet the above criteria must be reviewed by the convened IRB, as detailed in Section 7.B

Administrative Review of Amendments to Previously Approved Research

The IRB may use the Administrative Review of Amendments to Previously Approved Research in the following instances:

- Address, Telephone, Formatting Changes to Informed Consent Documents
- Approvals of Translated Documents which are accompanied by a Certificate of Translation

SECTION 13 – INVESTIGATIONAL DEVICE REVIEWS

Clinical investigations undertaken to develop safety and effectiveness data for medical devices must be conducted according to the requirements of the IDE regulations [21 CFR 812]. Certain clinical investigations of devices (e.g., certain studies of lawfully marketed devices) may be exempt from the IDE regulations [21 CFR 812.2(c)]. Unless exempt from the IDE regulations, an investigational device must be categorized as either "significant risk" (SR) or "non-significant risk" (NSR). If a SR determination is made, the IRB will notify the investigator and sponsor as well as record its determination in the meeting minutes.

The Code of Federal Regulations, Part 21CFR812.3 (m) uses the following definition:

> *Significant risk device* means an investigational device that:
>
> 1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
> 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.

A *Non-Significant Device* is one that does not meet any of the above criteria,

IRBs should note that where a protocol is subject to review under both FDA and DHHS human subjects regulations, both sets of regulations apply, and the requirements of both sets of regulations must be met.

The IRB must make a determination of SR or NSR for each device study that reviewed by the Convened Committee, except when exempt from IDE regulations. This determination must be recorded in the minutes of the Convened Committee Meeting.

I. 510(k) Devices

The review requirements for 510(k) devices are somewhat different. If FDA agrees that a new device is substantially equivalent to a device already on the market, it can be marketed without clinical testing. However, if clinical data are necessary to demonstrate equivalence, any clinical studies must be conducted in compliance with the requirements of the IDE, IRB review and informed consent regulations. Because 510(k) devices under clinical investigation fall under the IDE regulations, reporting of adverse or unanticipated 510(k) device effects follow the same requirements.

II. Humanitarian Device Exemptions

A Humanitarian Use Device (HUD) is a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year. FDA developed this regulation to provide an incentive for the development of devices for use in the treatment or diagnosis of diseases affecting these populations. The regulation provides for the submission of a humanitarian device exemption (HDE) application. An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury, and that the probable benefit to health outweighs the risk of injury or illness from its use. The labeling for an HUD must state that the device is a humanitarian use device and that, although the device is authorized by Federal Law, the effectiveness of the device for the specific indication has not been demonstrated. An approved HDE authorizes marketing of the HUD. However, a HUD may only be used after approval of the convened (full) IRB has been obtained for use of the device.

SECTION 14 – UNANTICIPATED PROBLEMS/ADVERSE EVENTS/IND AND PROTOCOL DEVIATION REPORTING

I. Procedures for Prompt Reporting and Review of Unanticipated Problems

Investigators are required to notify the IRB promptly of any unanticipated problems involving risks to subjects or others that occur in research conducted at NYP/Q or by NYP/Q's employees or agents. Any unanticipated problems must be reported to the IRB within using the Unanticipated Problems Involving Risk to Subjects or Others Reporting Form (**Appendix J**) within 2 weeks of the first awareness of their occurrence, whether such awareness is first attained by the Protocol PI.

An unanticipated problem involving risk to human participants or others is one that (1) was unforeseen at the time of its occurrence, and (2) indicates that participants or others are at an increased risk of harm.

Examples of non-serious unanticipated problems, including non-serious adverse events, that requiring reporting:

- Negative, non-life threatening physical reactions in a research participant to drugs administered in a study
- Physical consequences to a research participant from dietary manipulations (e.g., fainting)
- Negative, non-life threatening physical reactions in a research participant who has a chronic disease (e.g., diabetes, heart condition)
- Unanticipated accident to a research participant (e.g., participant's falling off a treadmill during an exercise study)
- Display of unanticipated emotional upset or degree of emotional upset by a research participant
- Accidental or unintentional change to the IRB-approved protocol that harmed research participants or others or that indicates that such persons may be at an increased risk of harm
- Release, including inadvertent release, of personal information of a research participant, or some other breach of confidentiality
- Occurrence that the sponsor requires be reported to it promptly
- Sponsor-imposed suspension for risk
- Acquisition of information that indicates a change to the risk-benefit analysis of the research, such as (1) an interim analysis or safety monitoring report indicating that frequency or magnitude of harms or benefits may be different from what was presented to the IRB; or (2) publication of a paper from another study showing that risks or potential benefits of the Cornell research study may be different from what was presented to the IRB.
- Failure of equipment during a study if such failure did or could have resulted in harm to a research participant
- Change to the protocol taken to eliminate an apparent immediate hazard to a research participant, without prior IRB review
- Complaint of a participant which indicates unanticipated risks or which cannot be resolved by the research team

If the reported occurrence is determined to be an unanticipated problem, as defined above the Report will be assigned for Expedited Review by the IRB Chair or/and IRB member with the relevant to an expertise. The Expedited Reviewer may require any action with respect to the protocol at issue, except that the following recommended actions except for: (1) modification of a protocol that was previously approved by the convened IRB; and (2) termination of a previously approved protocol. The Expedited Reviewer may, however, request the Chair of the IRB to suspend a protocol until the convened IRB reviews and acts on the protocol. The IRB Administrator will inform the Protocol PI of the IRB's determination If required, the Protocol PI will respond in writing to the IRB and this response will be reviewed by the Expedited Reviewer and/or the Chair of the IRB.

The review of an unanticipated problem can result in any of the following:

- Modification of the protocol
- Modification of the information disclosed during the consent process

- Providing additional information to past participants
- Notification to current participants when such information might relate to participants' willingness to continue to take part in the research
- Requirement that the current participants re-consent to participation
- Modification of the continuing review schedule
- Monitoring of the research
- Monitoring of any modified informed consent process
- Suspension of the research
- Termination of the research
- Referral to other organizational entities (*e.g.,* Institutional Biosafety Committee)
- Obtaining additional information
- Termination of a previously approved protocol, which occurs when the IRB permanently withdraws approval for all research activity

II. Procedures for Prompt Reporting and Review of Adverse Events

Investigators are also required to report promptly to the IRB any adverse event that is reported to the FDA or the sponsor in accordance with FDA requirements. An adverse event is any harm experienced by a participant regardless of whether the occurrence was on-site or off-site and which, in the opinion of the Protocol PI is both unexpected and related to the research. An adverse event is unexpected when its specificity and severity are not accurately reflected in the informed consent document.

If an adverse event occurs during the course of research involving human subjects it must be reported to the IRB within 5 business days of its occurrence by the completion of the Adverse Event Reporting Form (**Appendix I**), with any supporting information/documentation. Reporting is required regardless of whether the adverse event is serious or minor, was anticipated or unanticipated, or was study related or unrelated. In addition, for a multi-center study, it is required that the investigator provide copies of the reports of adverse events occurring at other study sites to the IRB within five business days of receiving the report.

The following serious adverse events requiring immediate reporting to the IRB within 24 hours of the first awareness of their occurrence, using the Adverse Event Reporting Form (**Appendix I**):

1. Death of a research participant
2. Serious injury to a research participant

The Chairperson of the IRB will initially review all adverse events and unanticipated problems originating from NYP/Q, and will determine if additional information is required from the investigator. The IRB will receive copies of either the Adverse Event Reporting Form (**Appendix I**), or the Unanticipated Problems Involving Risk to Subjects or Others Reporting Form (**Appendix J)** (and any additional material, if appropriate) and if deemed necessary, the reported will be forwarded for the next convened IRB meeting, at which time they will be discussed and voted upon as to the continuation, continuation with modifications/changes to the protocol/informed consent or the suspension of the protocol. This decision will then be noted in the minutes and reported back to the investigator.

The FDA believes that only the following adverse event should be considered as unanticipated problems that must be reported to the IRB:

- A single occurrence of a serious, unexpected event that is uncommon and strongly associated with drug exposure (such as angiodema, arganulocytosis, hepatic injury, or Stevens-Johnson syndrome).
- A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with drug exposure, but uncommon in the study population (e.g., tendon rupture, progressive multifocal leukoencephalopathy).
- Multiple occurrences of an adverse event that, based on an aggregate analysis, is determined to be an unanticipated problem. There should be a determination that the series of adverse events represents a signal that the adverse events were not just isolated occurrences and involve risk to human subjects (e.g., a comparison of rates across treatment groups reveal higher rate in the drug treatment arm versus a control). The FDA recommends that a summary and analyses supporting the determination accompany the report.
- An adverse event that is described or addressed in the investigators brochure, protocol, or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations. For example, if transaminase elevation is listed in the investigator's brochure and hepatic necrosis is observed in study subjects, hepatic necrosis would be considered an unanticipated problem involving risk to human subjects. The FDA recommends that a discussion of the divergence from the expected specificity or severity accompany the report.
- A serious adverse event that is described or addresses in the investigator's brochure, protocol, or informed consent documents, but for which the rate of occurrence in the study represents a clinically significance increase in the expected rate of occurrence (ordinarily, reporting would only be triggered if there were a credible baseline rate for comparison). The FDA recommends that a discussion of the divergence from the expected rate accompany the report.
- Any other adverse events or safety finding (e.g., based on animal or epidemiologic data) that would cause the sponsor to modify the investigator's brochure, study protocol, or informed consent documents, or would prompt other actions by the IRB to ensure the protection of human subjects. The FDA recommends that an explanation of the conclusions accompany the report.

If the reported occurrence is determined to be an serious adverse event, as defined above the Report will be assigned for Expedited Review by the The IRB Chair or and IRB member with the relevant to an expertise. The Expedited Reviewer may require any action with respect to the protocol at issue, except that the following recommended actions except for: (1) modification of a protocol that was previously approved by the convened IRB; and (2) termination of a previously approved protocol. The Expedited Reviewer may, however, request the Chair of the IRB to suspend a protocol until the convened IRB reviews and acts on the protocol. The IRB Administrator will inform the Protocol PI of the IRB's determination If required, the Protocol PI will respond in writing to the IRB and this response will be reviewed by the Expedited Reviewer and/or the Chair of the IRB.

The review of an unanticipated problem can result in any of the following:

- Modification of the protocol

- Modification of the information disclosed during the consent process
- Providing additional information to past participants
- Notification to current participants when such information might relate to participants' willingness to continue to take part in the research
- Requirement that the current participants re-consent to participation
- Modification of the continuing review schedule
- Monitoring of the research
- Monitoring of any modified informed consent process
- Suspension of the research
- Termination of the research
- Referral to other organizational entities (*e.g.,* Institutional Biosafety Committee)
- Obtaining additional information
- Termination of a previously approved protocol, which occurs when the IRB permanently withdraws approval for all research activity

III. Procedures for Prompt Reporting of IND Reports

Investigators are responsible for reviewing all IND safety reports sent by the sponsor. If the report meets item 1) above, the PI must submit a Notification of IND Safety Report (**Appendix K**) and include a copy of the IND safety report. If the report meets item 2) or item 3) above, the PI must submit a Request for IRB Review Form (**Appendix L**) and include a copy of the IND safety report). If the IND safety report does not represent an unanticipated problem or does not contain information that requires a change in protocol or consent form, the report does not have to be submitted. It should be kept by the investigator with the other regulatory documents provided by the sponsor

The Chairperson of the IRB will review IND reports from a multicenter study, and will make recommendation to the IRB as deemed necessary. The IRB has the authority to conduct site visits to promote research integrity if the IRB receives an excessive number of adverse events, or if the IRB independently suspects non-compliance or risks generated by the PI and/or the research team.

IND safety reports do not necessarily meet the definition of an unanticipated problem. Often, however, sponsors send IND safety reports to investigators and instruct the investigators to submit them to the IRB. The IND safety reports concern a product under study and such reports may not necessarily apply to events that occurred in the protocol conducted at NYP/Q.

The PI must submit IND safety reports to the NYP/Q IRB only in the following cases:

1. When the report meets the definition of an unanticipated problem
2. When an IND safety report triggers a sponsor-required change in the research protocol or consent form, or
3. When the sponsor indicates the safety information must be reviewed by the IRB to determine that either a change in research is required or currently enrolled subjects should be informed of the new information.

IV. Procedures for Prompt Reporting of Protocol Deviations

Regulation 45 CFR 46.103 and 21 CFR 56.113 requires the IRB to "follow written procedures for ensuring prompt reporting to the IRB…of…Any unanticipated problems involving risks to

human subjects or others...". Additionally, The GCP Guidance for Industry states that an investigator: should not implement any deviation from, or changes of, the protocol without agreement by the sponsor and prior review and documented approval opinion from the IRB of an amendment, except where necessary to eliminate an immediate hazard to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g., change of monitor(s), change of telephone number(s).

When a deviation from a protocol occurs the investigator is required to notify the IRB of said deviation, using the Protocol Deviation Form (**Appendix U**).The deviations must be reported within 10 days (5 days for major violations). The investigator must provide the IRB with the following information: if the deviation adversely affected the rights, safety or welfare of the subjects or significantly impacted the integrity of the research.

The investigator is required to notify the IRB of the date and description of the violation, explain how the deviation occurred , and the corrective actions to ensure that the same deviation will not occur in the future.

The IRB will determine if the deviation is a protocol exception (minor) or a protocol deviation (major); minor deviation is a logistical or administrative; major is a deviation that may impact the subject's rights, safety and welfare; the integrity of the data; or may substantially alter risks to research participants as determined by the IRB.

The IRB can choose to acknowledge the deviation; approve the deviations (for exceptions only or forward it for review by the full board. A full board review is necessary for repeated instances of continuous non-compliance (when investigators either avoid or ignore IRB policies,) and serious non-compliance. (Failure to comply with federal regulations, or failure to comply with IRB requirements or determinations)

For protocol violations that are considered continuous or serious non-compliance, the IRB can immediate suspend the protocol and notify the investigator in writing what must be done to correct the situation that lead to the violation and will also notify institutional officials of the deviation, including the IRB's corrective action. Non-response will constitute non-compliance and the research may be terminated or suspended. The IRB will report to the federal Office for Human Research Protections (OHRP), and any other sponsoring federal department or agency head, any serious or continuing noncompliance with the IRB requirements.

For serious non compliance, the IRB Chairman will immediately suspend the protocol and a summary of the violation, process, facts, and conclusions will be presented at the next scheduled Board meeting for further discussion and action. The IRB will notify the investigator in writing what must be done to correct the situation that lead to the violation and will also notify institutional officials of the deviation, including the IRB's corrective action. Investigators will have 15 calendar days to respond. Non-response will constitute non-compliance and the research may be terminated or suspended. The IRB will report to the federal Office for Human Research Protections (OHRP), and any other sponsoring federal department or agency head, any serious or continuing noncompliance with the IRB requirements.

V. Review of Data and Safety Monitoring Board (DSMB) Reports

Investigators are required to forward DSMB reports to the IRB within 5 working days of receipt. The review of DSMB reports is handled in the same manner as internal reports of

unanticipated problems or adverse events. When DSMBs are employed, the IRB when conducting continuing review of research may rely on a current statement from the DSMB indicating that it has reviewed study-wide adverse events, interim findings, and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB. Of course, the IRB must still receive and review reports of local, on-site unanticipated problems involving risks to subjects or others and any other information needed to make its continuing review substantive and meaningful.

VI. Reporting to Regulatory Agencies and Institutional Officials Regarding Serious Non-Compliance, Unanticipated Risks to others, and Terminations or Suspensions of Research

The IRB office will initiate these procedures if the IRB takes any of the following actions:

- Determines that an event may be considered an unanticipated problem involving risks to participants or others
- Determines that non-compliance was serious or continuing
- Suspends or terminates approval of research

The following information will be reported:

- The nature of the event (Unanticipated problem involving risks to participants or others, serious or continuing non-compliance, suspension or termination of approval of research)
- A detailed description of the problem including the findings of the organization and the reasons for the IRB's decision
- Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.)
- Plans, if any, to send a follow-up or final report by the earlier of a specific date

When an investigation has been completed or a corrective action plan has been implemented the IRB Chair and the Institutional Official review the letter and modify the letter as needed the Institutional Official signs the letter and returns it to the IRB Administrator or designee sends a copy of the report to:

- The IRB by including the letter in the next agenda packet as an information item
- The Institutional Official
- OHRP, if the study is subject to DHHS regulations or subject to a DHHS federalwide assurance
- FDA, if the study is subject to FDA regulations.
- If the study is conducted or funded by any Federal Agency other than DHHS that is subject to "The Common Rule", the report is sent to OHRP or the head of the agency as required by the agency (Reporting to a regulatory agency is not required if the event occurred at a site that was not subject to the direct oversight of the organization, and the agency has been notified of the event by the investigator, sponsor, another organization, or other mechanisms.)
- Chairman or supervisor of the principal investigator
- The Privacy Officer of a covered entity, if the event involved unauthorized use, loss, or disclosure of individually-identifiable patient information from that covered entity
- Others as deemed appropriate by the Institutional Official
- Principal investigator
- Sponsor, if the study is sponsored

SECTION 15 – ENROLLMENT CLOSURE OR STUDY CLOSURE

NYP/Q IRB requires that a Termination and Enrollment Closure Form (**Appendix O**) be submitted at the completion of every IRB approved study (exempt research is not applicable). Termination forms should be filed promptly and prior to expiration of IRB approval. If no termination form is received by the expiration date, NYP/Q IRB will issue an Expiration Letter, informing the investigator that no research activity may continue, and that the investigator has failed to meet continuing review obligations. Investigators who fail to file final reports may be subject to sanctions including, but not limited to, required additional education and training or suspension of investigator privileges.

It is the responsibility of the Investigator to ensure that the report is accurate and submitted in a timely fashion. Research projects should be closed when the following criteria are met:

1. Data collection is complete;
2. Study procedures are complete for subjects enrolled in the research project (i.e. phone calls, long term follow up, data collection visits, surveys are completed); and
3. Research activity is no longer being conducted at the site.

If an Investigator relinquishes his position as Principal Investigator for a project, he must notify NYP/Q IRB. If the Principal Investigator leaves his post at the investigational site without notifying NYP/Q IRB, NYP/Q IRB will seek a Notification of Enrollment Closure/Study Termination from a responsible party at the site to provide a final study report and to allow the IRB to safely close out the research project. If the study closes to enrollment, but research activity (e.g., subject follow-up, data analysis) continues, the Principal Investigator must notify NYP/Q IRB using the Termination and Enrollment Closure Form (**Appendix O**) . If the study is in the process of continuing review, then notification of the change in status from “actively enrolling” to “enrollment closed” can be done via the application for continuing approval.

SECTION 16 – MANAGING NONCOMPLIANCE IN HUMAN RESEARCH PROTECTION PROGRAM

Noncompliance occurs when research involving human participants is conducted in a manner that disregards or violates federal regulations, the policies or procedures of the Institutional Review Board (IRB), or institutional policies governing human research. Noncompliance with respect to human research participant protection violates NYP/Q’s Federalwide Assurance Registration (FWA). Even in the absence of intent, an unapproved or otherwise noncompliant research activity may place a research participant at unnecessary risk.

I. Terms and Definitions

Allegation: An assertion made by a party which has not yet been proven or supported by evidence.

Confirmed Noncompliance: An allegation of noncompliance that has been verified as a result of an investigation and/or a for-cause audit.

Continuing Noncompliance: A repeated pattern or un-rectified instance of noncompliance by an individual investigator or research staff member either on a single protocol or multiple protocols.

Noncompliance: Failure to comply with federal regulations; the policies or procedures of the Institutional Review Board (IRB); or institutional policies governing human research. Examples of noncompliance include: (1) conducting human participant research without IRB

approval (e.g., before approval; after expiration of approval and in the absence of a continuation application submitted to the IRB; during a suspension of IRB approval; after termination of IRB approval); (2) disregarding or otherwise violating IRB-approved informed consent procedures (e.g., failing to obtain consent/assent, using unapproved or outdated consent, assent, and information sheets, missing signatures, failing to document consent process); (3) deviating from the protocol approved by the IRB; (4) modifying an approved protocol without IRB consent; (5) failing to report or tardily reporting unanticipated problems; (6) failing to maintain adequate records; (7) failing to train research team members in the proper procedures; and (8) failing to follow recommendations by the IRB to ensure the safety of research participants..

Serious Noncompliance: Noncompliance involving one or more of the following: (1) bringing harm to research participants; (2) exposing research participants to a significant risk of substantive harm; (3) compromising the privacy and confidentiality of research participants; (4) causing damage to scientific integrity of the research data that has been collected; (5) engaging in willful or knowing noncompliance; (6) impacting ethical principles adversely.

II. Regulations Applicable to Managing Noncompliance

- 45 CFR 46.109; 21 CFR 56.109: IRB Review of Research, mandating IRB review and approval of human participant research.
- 45 CFR 46.103(b)(5)(i), mandating compliance with "[w]ritten procedures to ensure prompt reporting to the IRB, appropriate institutional officials, and the Department or Agency head of any serious or continuing noncompliance with [45 CFR 46(A)] or the requirements or determinations of the IRB."
- 21 CFR 56.108(b)(2), mandating compliance with "[w]ritten procedures to ensure prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of any serious or continuing noncompliance with [21 CFR 56(C)] or the requirements or determinations of the IRB."

III. Addressing Allegations of Noncompliance

The IRB may become aware of an allegation of noncompliance or of circumstances indicating noncompliance (See Section 15,Terms and Definition, Noncompliance) upon the receipt of a complaint from a participant, researcher, NYP/Q employee, or member of the public; from the interpretation of information received during a Continuation, Amendment, Unanticipated Problems Review; or from the findings of a random or for-cause audit or other quality control activities.

Once it has received an allegation of noncompliance, the IRB Administrator will request the alleger to submit a memo to the IRB. In the case of an anonymous complaint or a request for confidentiality, the IRB Administrator will submit this form. The IRB Administrator will forward the form to the IRB Chair and the Institutional Official for review. The IRB Chair and the Institutional Official will make the following initial determinations: (a) whether noncompliance is alleged; and (b) whether the allegation indicates that an immediate action such as suspension by the IRB is warranted. If it is determined that immediate action by the IRB is warranted (*e.g.,* suspension), then the IRB Chair will initiate those proceedings.

The IRB will then initiate an investigation of the circumstances alleged in the Noncompliance Report Memo. The IRB may elect to investigate informally by reading relevant documents and communicating with the affected parties. If the IRB Chair determine that the allegation is not credible or is unsubstantiated, then the inquiry ends. The IRB Administrator will document this finding in a written report; place the report in the study file; and notify the IRB of the finding on the agenda of the next available meeting. If, however, the inquiry yields evidence that

noncompliance has occurred, then the IRB Administrator will present this information to the IRB Chair and submit a corresponding report to the full IRB for discussion at the next available meeting.

IV. Confirming and Resolving Noncompliance

If it is determined that the noncompliance is neither serious nor continuing (See Section 15, Terms and Definitions), the IRB Committee will devise a corrective plan, which generally will involve immediate remediation (e.g., obtaining signature of Protocol PI on submissions, providing missing documentation) and/or remedial education with the IRB Administrator.

If it is determined that the noncompliance is serious or continuing, The IRB Administrator will conduct a for cause audit If it is determined that an unanticipated problem has occurred, the IRB Chair will address it.. The Protocol PI may request a meeting with the IRB Chair or the Committee regarding their determination of serious or continuing noncompliance. The Protocol PI may decide voluntarily to suspend or terminate some or all of the research activities that may be under current review or investigation. The Protocol PI should inform the IRB Administrator of this action, so that they can notify the IRB Chair and place the protocol on the agenda for the next available IRB meeting.

The IRB Administrator will distribute its for-cause audit report to the Protocol PI, the IRB Chair, the members of the IRB, and the Institutional Official and/or Chair of the Protocol PI's Department. The Protocol PI may submit a response to the audit report in writing and/or may request to speak to the IRB at a convened meeting. The IRB Administrator will place the report and any written response from the Protocol PI as discussion items on the agenda of the next available IRB meeting. The IRB will make a final determination as to whether the evidence supports a finding of serious or continuing noncompliance and, if so, will determine a corrective plan, including timeframe for correction, and will, if necessary, initiate suspension or termination proceedings.

In reviewing information to make a final determination of serious or continuing noncompliance, the IRB should consider:

1. Whether the audit report and any other available information sufficiently supports a determination of non-compliance
2. Whether the audit report and any other available information supports suspension or termination of research in order to protect human participants or others
3. Additional actions to protect the rights and welfare of currently enrolled participants
4. Whether procedures for withdrawal of enrolled participants account for their rights and welfare
5. Whether participants should be informed of the noncompliance and/or any of the corrective actions

The IRB may invite the Protocol PI to a portion of the meeting to answer questions and to discuss the issue of noncompliance. If the Protocol PI requests, or is requested, to be present at the IRB meeting, he or she may be accompanied by a faculty representative, legal counsel, or another member of his or her department. The role of these individuals is limited to providing information and support to the Protocol PI; they will not participate in the discussion between the Protocol PI and the IRB.

The Protocol PI must implement the corrective plan within the required timeframe. The IRB Administrator will monitor the Protocol PI's implementation of the corrective plan. A failure to implement the corrective plan on time will be reported to the IRB Chair and the Institutional

Official for further action, including initiation of procedures for suspension or termination of IRB approval of the research protocol.

Upon full implementation of the corrective plan, the IRB Administrator will draft a final noncompliance report for discussion by the IRB at the next available meeting. . After the report is finalized by the convened committee and the Institutional Official, the IRB Administrator will distribute this report to the following parties:

1. Protocol PI
2. Department Chair, of the Protocol PI
3. Legal Affairs, when applicable
4. Sponsoring agency, when applicable
5. OHRP, when applicable

While the IRB has the authority to take appropriate action concerning a research protocol, neither the IRB Chair nor committee has the authority to take disciplinary action against any individual relating to a finding of confirmed noncompliance. Instead, disciplinary action shall be the responsibility of the Institutional Official.

V. Corrective Actions in Response to Noncompliance

The actions taken to correct noncompliance vary and depend on the nature and seriousness of the noncompliance. The IRB, may take any of the following actions:

- Take no action
- Request a protocol and/or consent form modification
- Require that all participants be re-consented
- Require previous participants to be informed of any changes to the protocol and/or
- consent procedures
- Require observation of consent procedures
- Require more frequent review of the conduct of the research
- Require additional training for the research team
- Require follow-up audit(s)
- Suspend the research:
- Terminate the research:
- Any other action deemed appropriate by the IRB to protect the rights and welfare of research participants
- Informed by any audit reports, corrective plans, and final noncompliance reports, the IRB Administrator will develop and administer required and optional educational programs, as specified in corrective plans for the Protocol PI and for the research community generally.

VI. Documentation Relating to Reporting and Resolution of Noncompliance

All documents relating to noncompliance will be maintained by the IRB Administrator for a period of not less than 5 years, in accordance with Introduction Section: IRB Record Keeping. These documents include but are not limited to: Noncompliance Report Forms; correspondence with the Protocol PI; and documentation of implementation of corrective plans.

SECTION 17 – REVIEW OF RESEACH INCLUDING CHILDREN

Under the federal regulations, children are “persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in

which the research will be conducted." For research in New York State, individuals under the age of 18 are considered to meet the DHHS and FDA definitions of "children." This includes not only viable neonates, but also college and university students under the age of 18, unless a waiver is approved by the IRB. New York State does not recognize the concept of an "emancipated minor" for the purposes of research. If investigators are recruiting children outside of New York State, the Protocol PI must report this category of participant in the protocol and state the definitions of child, parent, and legal guardian in that jurisdiction.

Children are a "vulnerable population," because they are considered easily susceptible to coercion and undue influence and incapable of completely understanding the risks and benefits in making the decision to participate in research. The respect for persons elaborated in the Belmont Report requires that the decision to participate in research be wholly informed and voluntary. The IRB recognizes the importance of conducting scientifically sound research and ethically designed studies in this population. Excluding them from participating in the research is not an answer. Instead special precautions should be incorporated into the design of the study to protect the rights and welfare of child participants.

When children are involved, the IRB gives special consideration to recruitment methods, oversight of the consent/assent processes, and the completeness of information provided to the child's decision-maker. The extent of protection of the child's rights and welfare considered by the IRB depends on the risk of harm and the likelihood, the degree of the benefit to the child from involvement in the study, and the age range of the children who are being asked to participate. This policy discusses these special considerations and protections.

Moreover, in order to safeguard their interests and to protect them from harm, federally-mandated considerations are in place for reviewing research involving children. Adding to the protection provided under the Common Rule (45 CFR 46), federal regulations (45 CFR 46, Subpart D) provide protections for children involved in research such as obtaining assent from the child and obtaining the permission of the parents/legal guardians for the child to be enrolled in the research protocol

I. Categories of Permissible Research Involving Children

Federal regulations require the IRB to classify research involving children into one of three categories and to document the discussions of the risks and benefits of the research study. The IRB Minutes should document how the research protocol meets its assigned category. These are the three categories of permissible research, based on the degree of risk and benefit to the child:

1. **Research not involving greater than minimal risk (45CFR46.404)**
   Children can be approved for these studies only when the IRB finds that adequate provisions have been made for soliciting the assent of the children and the permission of their parents or legal guardians to participate in the research study. Permission from one parent/guardian is sufficient for Category 1 research, unless this is contradictory to the regulations of the U.S. or foreign jurisdiction in which the research is being conducted.

2. **Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual participants (§46.405)**
   Children can be approved for these studies only when the IRB finds that: (1) the risk is justified by the anticipated benefit to the participants; (2) the relation of the anticipated benefit to the risk is at least as favorable to the participants 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 legal guardians to participate in the research study. Permission from one parent/guardian is sufficient for Category 2, unless this is contradictory to the regulations of the U.S. or foreign jurisdiction in which the research is being conducted.

3. **Research involving greater than minimal risk and no prospect of direct benefit to individual participants, but likely to yield generalizable knowledge about the participants' disorder or condition (§46.406)**
Children can be approved for these studies only when the IRB finds that: (1) the risk represents a minor increase over minimal risk; (2) the intervention or procedure presents experiences to participants 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 participants' disorder or condition which is of vital importance for the understanding or amelioration of the participants' disorder or condition; and (4) adequate provisions are made for soliciting assent of the children and permission of their parents or legal guardians to participate in the research study.

For Category 3, both parents must give parental permission. When there is disagreement between both parents, the child may not be enrolled in the research study. However, only one signature of a parent is required when the second parent is deceased, unknown, incompetent, or not reasonably available (e.g., no contact with child, serving in war, in solitary confinement or otherwise hard to reach in prison), or if one parent has the legal responsibility for the care and custody of the child, as long as this comports with the regulations of the U.S. or foreign jurisdiction in which the research is being conducted. The reason for the allowance of only one parental signature should be documented in the research records.

II. Wards of the State:

The special protections for children set forth in 45 CFR 46, Subpart D, addressing children, include additional limitations on some research involving children who are wards of the state or any other agency, institution, or entity. When the research involves greater than minimal risk to the participants with no prospect of direct benefit to individual participants (Category 3), the research must either relate to their status as wards or else be conducted in schools, camps, hospitals, institutions, or similar settings where the majority of participating children are not wards. The IRB requires for each ward the appointment of an advocate in addition to any other individual acting on behalf of the child as a parent, legal guardian, or other legally authorized representative

III. Determination by IRB of Probable Risks and Associated Discomforts:

The IRB is required to consider the following when reviewing research involving children: (1) probable risks; (2) associated discomforts; and (3) potential benefits. Procedures that usually present no more than minimal risk to a healthy child include: urinalyses, obtaining small blood samples, EEGs, allergy scratch tests, minor changes in diet or daily routine, and/or the use of standard psychological and educational tests. The assessment of the probability and magnitude of the risk, however, may be different in sick children and vary depending on the diseases or conditions afflicting the participant. For example, obtaining a small blood sample from a hemophiliac child may present more than minimal risk to him or her. The IRB must also consider the extent to which research procedures would burden any child, regardless of whether the child is accustomed to the proposed procedures. Procedures that exceed the limits of minimal risk may be difficult to define in the abstract, but should not be too difficult to

identify on a case-by-case basis. For example, behavioral interventions may, in some circumstances, exceed minimal risk.

IV. Determination by IRB of Potential Benefits:

In assessing the potential benefits of a research intervention, the IRB, again, should consider the variability in health statuses among the potential participants. For example, a potential participant might be a normal, healthy child, or a child who has been exposed to a disease or a toxin (e.g., lead) or some psychological upset or trauma. A child may also suffer from a medical condition. The IRB must take into account the current health status (mental and physical) of a child and the likelihood of progression to a worsened state without (or with) the research intervention.

V. Procedures for Obtaining Permission from Parent(s) and Assent from the Child

The Protocol PI generally should obtain permission from parents *before* approaching a child. In most cases, after parental permission has been obtained and documented, the assent of the child is required. Enrollment of children in a research protocol requires the Protocol PI's consideration of the steps set forth in this Section for obtaining permission from the parent(s) and the assent from the child.

"Assent" in research involving children means a child's affirmative agreement to participate in the research. Mere failure to object cannot be construed as assent. "Permission" in research involving children means the agreement of the parent(s) or legal guardian to the participation of their child or ward in the research. "Parent" means a child's biological or adoptive parent. "Legal Guardian" means an individual who is authorized under applicable New York State law to consent on behalf of a child to general medical care.

A child may be under the care of a family member who serves as the child's primary caregiver. While such primary caregivers may be eligible to provide permission for more clinical type activity, they are not legally authorized to enroll their minor charges in a research project, regardless of whether it meets Categories 1, 2, or 3 outlined in 13A of this policy, unless a court has appointed them as the child's legal guardian.

VI. Permission of the Parent(s)/Guardian(s):

If children are eligible to be enrolled in a research protocol, parental permission is generally required for each of the three categories of permissible research outlined in 13A of this policy, before the child is approached for his or her assent. Permission by parents or guardians shall be documented in accordance with and to the extent required by MOP 9.

However, the IRB has the authority to waive the requirement for parental permission (a) under the same conditions that it can waive informed consent (Section 9), and (b) if it determines that a research protocol is designed for conditions or for a participant population for which parental or guardian permission is not a reasonable requirement to protect the participants (e.g., neglected or abused children are participants or research protocol poses minimal risk and parental/guardian permission would provide no additional protection from risks), provided an appropriate mechanism for protecting children who will participate in the research is substituted, if appropriate, and 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 participating children, and the children's age, maturity, status, and condition.

If the child has a legal guardian, the Protocol PI should maintain in the child participant's

file legal documentation showing the decision-maker's status as the child's legal guardian.

VII. Assent of the Child:

1. Children cannot consent to participate in research themselves. Therefore, parental permission and the assent of the child must be obtained. There are no regulatory standards for assent outside of the statement in 45 CFR 46.408, requiring the IRB to "determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate."

2. However, there are three exceptions to the need to obtain the assent of the child:
    a. The IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted.
    b. The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research.
    c. The IRB determines that the child participants are capable of assenting, but the situation presents circumstances in which the IRB may waive the consent requirement, as set forth in (Section 9),or otherwise. However, for some types of research where documentation of informed consent would normally be waived (such as surveys), the IRB may require documentation for children.

3. Assent is documented depending on the age, maturity, and psychological state of the child. All of the forms/documents pertaining to the study should be submitted by theProtocol PI as part of the protocol application for IRB review and approval.
    a. Age under 7 years, assent is waived or oral assent is obtained, as determined by the IRB
    b. Age 7-12 years, oral assent is recommended; but a written statement of information can be used to provide information about the study to the child when appropriate; a copy of the oral assent script should be submitted with the protocol; parental permission forms should have a line for documenting oral assent and should be signed by the person obtaining assent.
    c. Age 13-17 years, written assent should be obtained by a document that is written at an appropriate reading level. If the parental permission form is written at a grade level that is understandable for children ages 13-17, the Protocol PI may add a line for child assent and use the form for documenting both the child's assent and parental permission. However, separate assent and consent forms may be required if the language in the consent form is so complex that the child may not be able to understand it.

    The IRB may waive the documentation requirement where the assent document would be the only link between the participant and the research and would pose a confidentiality risk. (Section 9*),*

4. Participants who were enrolled in research studies when they were minors must be reconsented when they turn 18 years old if they are still participating actively in the study. The Protocol PI should follow the procedures for re-consenting participants set forth in Section 9e and 9f)

5. In general, a child's dissent should be respected. However, a child's assent cannot override a "no" from a parent, unless the IRB has waived the requirement for parental permission. Ordinarily, a disagreement between parent(s) and child may arise because the child is depressed, the parents have unrealistic hopes, the child has different goals and outcomes than the parent(s), or the risk/benefit ratio has been misunderstood. Every effort should be made to reach consensus between the parent(s) and child. However, when the research offers the child the possibility of direct benefit important to his/her own health and may be available only through research (Category 2), the parent(s)' wishes generally prevail over the child's dissent.

VIII. Documentation of IRB Review

IRB Administrator will document in the meeting minutes the outcome of any IRB discussion related to the enrollment of children in the protocol, Including but not limited to:

1. Federally required considerations per 45 CFR 46, Subpart D
2. Consent/Assent process
3. Re-consent timing and procedures, if any
4. Protocols that include children may be reviewed for Continuation by the IRB more often than every 12 months per the determination of the IRB.

SECTION 18 – GUIDANCE FOR REVIEW OF RESEARCH INCLUDING PRISONERS

While a person's status as a prisoner does not bar his or her participation in research, such participation and the associated research warrant additional scrutiny by the IRB. Under the federal regulations, prisoner "means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing." The definition applies to minors as well as adults.

I. Categories of Permissible Research Involving Prisoners

A research protocol that involves prisoners may not qualify for exemption from IRB review. Where the study carries greater than minimal risk, a potential benefit to society or the convenience of prisoners as a study population is an insufficient justification for their enrollment. In addition to the approval criteria applicable to all human participant research, the IRB shall approve research involving prisoners only if it meets the following criteria.

The research under review represents one of the following permissible categories of research:

- 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 participants;
- Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the participants;
- Research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults), provided that the study may proceed only after the HHS Secretary has consulted with appropriate experts including experts in penology, medicine, and ethics, and has published notice in the Federal Register of his intent to approve such research; or

- Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the participants. In cases where those studies require the assignment of prisoners, in a manner consistent with protocols approved by the IRB, to control groups that may not benefit from the research, the study may proceed only after the HHS Secretary has consulted with appropriate experts, including experts in penology, medicine, and ethics, and has published notice in the Federal Register of the intent to approve such research.
- 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. Involvement in a research protocol cannot be considered during a parole hearing for any prisoner who has agreed voluntarily to be a research participant;
- The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
- Procedures for the selection of participants within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the PI provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for participants in that particular research project;
- The information is presented in language that is understandable to the participant population;
- 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
- Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

SECTION 19 – GUIDANCE FOR REVIEW OF RESEARCH INCLUDING PREGNANT WOMEN OR FETUSES

I. Definitions

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

(a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

(b) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;

(c) Any risk is the least possible for achieving the objectives of the research;

(d) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of subpart A of this part;

(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 subpart A of this part, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

(f) Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

(g) For children as defined in §46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part;

(h) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

(i) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

(j) Individuals engaged in the research will have no part in determining the viability of a neonate.

II. Research Involving Neonates

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

- Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
- Each individual providing consent under paragraph (b)(2) or (c)(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
- Individuals engaged in the research will have no part in determining the viability of a neonate.
- The requirements of paragraph (b) or (c) of this section have been met as applicable.

III. Neonates of Uncertain Viability

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

- The 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
- 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
- The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the

legally effective informed consent of either parent's legally authorized representative is obtained in accord with subpart A of this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

IV. Nonviable neonates

After delivery nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met:

- Vital functions of the neonate will not be artificially maintained;
- The research will not terminate the heartbeat or respiration of the neonate;
- There will be no added risk to the neonate resulting from the research;
- The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
- The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of this part, except that the waiver and alteration provisions of §46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest.

V. Viable Neonates

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the Federal Regulation and Guidance

VI. Research Involving, after Delivery, the Placenta, the Dead Fetus or Fetal Material

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

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

VII. Research not Otherwise Approvable which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Pregnant Women, Fetuses, or Neonates

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

1. That the research in fact satisfies the conditions of Pregnant women and fetuses, as applicable

2. The following:

(i) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;

(ii) The research will be conducted in accord with sound ethical principles; and

(iii) Informed consent will be obtained in accord with the informed consent provisions and other applicable sections of this policy.

SECTION 20 – INTELLECTUAL PROPERTY

NYP/Qs (the "Hospital) may assert ownership in intellectual property of all types resulting from Hospital Research (including, but not limited to , any invention, discovery, trade secret, technology, scientific to technological development, computer software and business method) regardless of whether this intellectual property is subject to protection under patent, trademark, copyright or other laws. Hospital Research shall be defined, for purpose of this policy, to include all research conducted or discoveries made in the course of an inventor's employment with the Hospital or with the use of Hospital resources. Hospital resources include, but are not limited to, Hospital funds, facilities, space or time of the employee. Inventions conceived or first reduced to practice in furtherance of Hospital research of staff, or discoveries made, shall be promptly disclosed in writing to The Theresa & Eugene M. Lang Center for Research and Education. All patentable inventions conceived or first reduced to practice by Hospital staff in the conduct of Hospital research shall belong to the Hospital. The Hospital shall be responsible for prosecuting, litigating and marketing the patent, including the costs thereof. Subject to the Hospital Copyright Policy, the inventor or creator shall cooperate and assist the Hospital in all phases of the patent, trademark and/or copyright application process and shall assign such applications or any patents, trademarks or copyrights resulting there from to The Theresa & Eugene M. Lang Center for Research & Education. If the Hospital declines to elect title, or if having elected decides not to pursue further development, prosecution, litigation or marketing of an intellectual property, then, at the request of either party, the Hospital may assign back title to the inventor/creator of the intellectual property. Patentable inventions made by individuals on their own time and without the use of Hospital resources shall belong to the individual inventor. Disputes concerning ownership or disposition of intellectual property which remain unresolved shall be determined by the President and CEO of the Hospital with the advice of The Theresa & Eugene M. Lang Center for Research & Education (Advisory Board) and in consultation with the Board of Trustees.

I. Royalty Distribution

In the event that the Hospital transfers or licenses the intellectual property for commercial development, and in recognition of the efforts and contributions of the inventor, fifty percent (50%) of the total net payments or royalty income shall be distributed to the inventor. The remaining fifty percent (50%) shall be retained by the Hospital's Theresa & Eugene M. Lang Center for Research & Education.

Net payments and royalty income shall be defined as gross payments and royalty income less directly assignable expenses resulting from patenting, licensing, or otherwise protecting or marketing the particular intellectual property.

SECTION 21 – USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION FOR RESEARCH PURPOSES

The Privacy Rule defines individually identifiable health information transmitted or maintained by

a covered entity in any form (electronic, written or oral) as "protected health information" (PHI) and establishes the conditions under which investigators may access and use this information in the conduct of research. PHI is any information that relates to the past, present or future physical or mental health or condition of an individual who can be identified by any of eighteen specific identifiers (name, geographic location smaller than a State or the first three digits of a ZIP code, dates except year, telephone number, fax number, e-mail address, social security number, medical record number, health plan beneficiary numbers, account numbers, certificate or license numbers, vehicle identifiers and serial numbers, device identifiers and serial numbers, URLs, Internet protocol (IP) address numbers, biometric identifiers, full face photographs, any other unique identifying number, characteristic or code (45 CFR 164.514(b)(2)(i)). Health information in this context includes biological specimens if they can be individually identified.

With the implementation of the Privacy Rule, research involving humans as research participants must be conducted according to three sets of regulations.

2. Investigators doing research involving a product regulated by the Food and Drug Administration (FDA) are required to meet all relevant FDA regulations. Such research ordinarily involves the use of a drug, device or biological product, whether the regulated product has received FDA approval for marketing or remains an investigational product. Regulations describing the need to protect the research subject's privacy are set forth in 21 CFR 56.111(a)(7). This citation also notes the need for ensuring the confidentiality of the subject's data, as do regulations set forth in 21 CFR 50.25(a)(5).

3. If the investigator receives U.S. federal funds to support his/her research, or if the investigator is a faculty or staff member of an academic institution that has made a commitment to the U.S. Department of Health and Human Services (DHHS) to follow all federal regulations governing research involving humans subjects, the investigator is required to comply with regulations set forth in 45 CFR 46, including subparts A-D. Subpart A, titled "Basic HHS Policy for Protection of Human Research Subjects", is referred to as the Common Rule. Regulations describing the need to protect the research subject's privacy are set forth in 45 CFR 46.111(a)(7). This citation also notes the need for ensuring the confidentiality of the subject's data, as do regulations set forth in 45 CFR 46.101(b)(3), 46.116(a)(5) and 46.117(c)(1).

4. Investigators in institutions that meet the definition of a covered entity must also comply with the Privacy Rule. The regulations described above are unchanged by the Privacy Rule. While they provide for protection of the research subject's privacy and for the confidentiality of his/her research data, such protections are enhanced by the Privacy Rule (45 CFR 160 & 164). It adds a layer of privacy protections for subjects by defining the ways in which a person's individually identifiable health information may be used in research.

I. Authorization

Except as otherwise permitted, the Privacy Rule requires that a research subject "authorize" the use or disclosure of his/her PHI to be utilized in the research. This authorization is distinct from the subject's consent to participate in research, which is required under the Common Rule and FDA regulations. Just as a valid consent under Common Rule and FDA regulations must meet certain requirements, a valid authorization must contain certain core elements (45 CFR 164.508(c)). The subject must authorize specifically what research information may be shared and who will receive the information, must acknowledge the expiration of the authorization and have the right to revoke the authorization, and must be informed that further disclosure by recipients of the information may not be covered by the federal privacy rules. In keeping with NYP/Q IRB policy, this authorization is to be incorporated into the informed

consent document. The subject's right to revoke authorization is limited. The investigator and the institution may continue to use and disclose PHI that was obtained before the subject revoked authorization to the extent that the investigator or institution has acted in reliance on the authorization, such as to use or disclose PHI in order to maintain the integrity of the research (45 CFR 164.508(b)(5)(i)).

A sample consent and authorization form, which includes HIPAA language, is located in **Appendix P.**

II. Compliance Committee

The Privacy Rule (45 CFR 164.512(i)(1)(i)(B)) describes a new board, constituted in a manner similar to an IRB, that has authority to implement the Rule as it relates to alteration of authorization or waiver of authorization. The IRB has responsibility for enforcing HIPAA regulations at New York Presbyterian/Queens, as they apply to research projects.

The HIPAA regulations require clinical protocols to discuss how the privacy of patients will be protected regarding the future use of their health information as well as the storage of their health information. These are referred to as research authorizations.

Protected health information obtained by the hospital may not be used internally or disclosed to any persons or organizations outside the hospital for research purposes without the prior approval of the hospital's Institutional Review Board The Institutional Review Board may designate one or more persons to act on his or her behalf in any or all aspects covered by this policy. All requests for access to protected health information for research purposes must be made and reviewed in accordance with the procedures explained below and forwarded to the Institutional Review Board The Institutional Review Board will be responsible for ensuring that strict policies and procedures regarding the access, use, and disclosure of protected health information for research purposes are followed. This means that no research may be conducted by any hospital staff or on the hospital's premises without the prior approval of the Institutional Review Board.

III. Implementation of Policy

Certain requirements apply to the use and disclosure of protected health information in connection with all research involving human subjects. As a general rule, the Institutional Review Board may not authorize the use or disclosure of protected health information for research purposes except:

- for reviews preparatory to research;
- for research on the protected health information of a decedent;
- if the hospital has a consent form for the specific research project signed by the individual prior to April 14, 2003;
- if the information is "de-identified;"
- if the hospital has obtained the individual's authorization; or
- if the Institutional Review Board (IRB) or a Privacy Board approves a waiver of individual authorization.

Special rules apply to the use and/or disclosure for research purposes of the following types of information:

- genetic tests and results from genetic tests;
- HIV-related information

The IRB must determine that one of the exceptions described below applies before permitting the use or disclosure of any protected health information for research purposes. The IRB should require either authorization or a waiver if he or she has any doubt about whether any other exception is applicable. All hospital research activities must also comply with other applicable hospital policies relating to and with any additional requirements that apply to the specific types of information identified above as having special rules. Finally, to the extent medical staff and hospital staff provide treatment to subjects as part of a research study, they must follow other hospital policies to the extent those policies apply to the provision of health care to individuals

The IRB may not authorize the use or disclosure of protected health information for research purposes unless at least one of the following exceptions applies:

IV. Reviews Preparatory to Research

The IRB may permit the use and disclosure of protected health information to develop a research protocol or for similar purposes preparatory to research (*e.g.*, to determine whether the hospital has information about prospective research participants that would meet the eligibility criteria for enrollment in a research study). Researchers should be aware that this exception does *not* permit the continued use or disclosure of the protected health information once the Principal Investigator has determined to go forward with the study. For example, using protected health information to contact eligible subjects for recruitment purposes would *not* be permitted under this exception.

In order to permit a use or disclosure of protected health information under this exception, the Principal Investigator must submit a Notification Of A Review Preparatory To Research form (RPR) (**Appendix Q**).

- This RPR form must only be used if PHI will be reviewed, **but not recorded**, prior to subject consent.
- If PHI will be recorded prior to subject consent, whether or not the PHI will leave NYP/Q, the PI must complete a Request for a Waiver of Consent and HIPAA Authorization (**Appendix H**).
- In order to comply with the Privacy Rule (HIPAA), this RPR form must be used only if PHI will not leave NYP/Q. If PHI will leave NYP/Q without subject authorization, you need to complete a Request for a Waiver of Consent and HIPAA Authorization (**Appendix H**).
- If identifiable private information other than PHI will be recorded prior to subject consent, you must complete a Request for a Waiver of Consent and HIPAA Authorization (**Appendix H**).

During the preparatory review, those granted access may only record information in a form that is “de-identified.” Please refer to 18 HIPAA Identifiers (**Appendix R**) to learn more about what information is considered de-identified.

As described above (Review Preparatory to Research), NYP/Q has provided guidance that it considers research to be occurring if the investigator records PHI or other identifiable private information during the search for potential subjects (during the ascertainment/recruitment process). The investigator must therefore first obtain IRB approval of the research, and then obtain either consent and authorization of the subjects or IRB approval of a waiver of consent

and authorization.

Waiver of consent under the Common Rule (45 CFR 46.116(d)) requires that the IRB find that:

- The research involves no more than minimal risk.
- The waiver does not adversely affect the rights and welfare of the subject.
- The research could not be practicably carried out without the waiver.
- Whenever appropriate, the subjects will be informed of any pertinent information.

In order for the IRB also to alter or waive authorization, the Privacy Rule (45 CFR164.512(i)(2)(ii)) requires that the IRB find that:

- Disclosure of the PHI involves no more than minimal risk.
- The waiver will not adversely affect the privacy rights or welfare of the subject.
- The research could not practicably be carried out without the waiver.
- The research could not practicably be carried out without access to the PHI.
- The privacy risks are reasonable in relation to the information to be gained.
- There is an adequate plan to protect the identifiers from improper use and disclosure.
- There is an adequate plan to destroy the identifiers at the earliest opportunity.
- There is written assurance that the PHI will not be further disclosed, with a few exceptions specified in 45 CFR 164.512(i)(2)(ii)(A)(3).

When requesting waiver or alteration of authorization, use the form found on the forms page of the IRB web site. When requesting both waiver of consent and waiver of authorization, use the form found on the forms page of the IRB web site.

V. Guidelines for Pre-Screening Subjects for Recruitment (Databases & Repositories)

A. Databases and Repositories

The Privacy Rule recognizes the creation of a research database or a specimen repository to be a research activity if the data/specimens stored contain PHI: http://privacyruleandresearch.nih.gov/

Similarly, each use or disclosure of PHI from a database or repository for research purposes is considered a separate research activity. The Privacy Rule does not permit authorization to be given for unspecified future research. Thus the authorization to include PHI in a database and/or specimen repository must specify the research purpose for which the use or disclosure will occur (in this case, the storage in the research database or specimen repository). As with any authorization, this one may either be combined with an IRB approved consent for research or obtained as a separate document, although NYP/Q IRB policy requires investigators to integrate the authorization contents into the consent document.

Furthermore, research-related treatment cannot be conditioned on participation in future unspecified research, such as the collection and storage of data/samples for future vague research. Requesting authorization from a research subject for the use or disclosure of his/her data/specimens for future unspecified research is precluded. Requesting authorization from a research subject for the use or disclosure of his/her data/specimens for current or future specified research is permitted.

Banking (i.e..- Registry Studies) within NYP/Q of data/specimens for future research related to the subject's disease, or to any human disease, but not clearly related to the purpose of this research protocol, would be permitted only if the banking request were a separate request that complies with the NYP/Q policy on data/sample repositories.

As noted below, all future research uses and disclosures of PHI from a database or specimen repository require IRB approval. The IRB may require re-consent/authorization if the intended purpose of the future research is outside the original intent of the database/repository. Or, alternatively, the IRB may waive consent and authorization if the requirements for waiver of each are met. Anonymization and deidentification of the data or release as a limited data set with a data use agreement (discussed below) are alternative considerations that may be useful in certain circumstances.

The potential subject's permission to be contacted must be obtained prior to direct contact by study staff. Those subjects who respond to advertisements or recruitment letters have implicitly given their permission to be contacted.

Questions during pre-screening should address the research project's inclusion/exclusion criteria and other issues related to the potential subjects participation in the research, such as, the ability to come to the research site multiple times. Pre-screening should not include gathering specific information about an individual's medical history or any other specific details of the individual's condition. Such information should only be solicited once informed consent is obtained and the subject is enrolled in the research project.

B. Limited Data Set with a Data Use Agreement

The Privacy Rule also introduces a strategy for presenting PHI, such as PHI in a database with or without an associated sample repository, as a limited data set with a data use agreement, thereby fulfilling Privacy Rule requirements (45 CFR 164.514(e)). The PHI can be presented as a limited data set by removing all direct personal identifiers, and removing postal address information except for town or city, State and ZIP code (nine digit ZIP+4 code is permitted). Event dates, the subject's age (without restriction) and an identifying code derived from the subject's PHI (such as subject initials) may be included in the limited data set. Therefore data in a limited data set are not de-identified data.

C. Limited Data Set

PHI that excludes the following direct identifiers of the individual or of relatives, employers, or household members of the individual. Requires a Limited Data Use Agreement (**Appendix T**) and needs Institutional Review Board (IRB) review:

- Name;
- Postal address information, other than town or city, State, and zip code;
- Telephone numbers;
- Fax numbers;
- Electronic mail addresses;
- Social security numbers;
- Medical record numbers;
- Health plan beneficiary numbers;
- Account numbers;

- Certificate/license numbers;
- Vehicle identifiers and serial numbers;
- Device identifiers and serial numbers;
- Web Universal Resource Locators (URLs);
- Internet Protocol (IP) address numbers;
- Biometric identifiers, including finger and voice prints; and
- Full face photographic images and any comparable images

A limited data set could include the following (potentially identifying) information:

- admission, discharge, and service dates;
- dates of birth and, if applicable, death;
- age (including age 90 or over); and
- five-digit zip code or any other geographic subdivision, such as state, county, city, precinct and their equivalent geocodes (except street address).

D. Data Use Agreement

An agreement required by the Privacy Rule between a covered entity and a person or entity that receives a limited data set. The Data Use Agreement must state that the recipient will use or disclose the information in the limited data set only for specific limited purposes. Must accompany a Limited Data Use Agreement (**Appendix T**).

A data use agreement must be in place to ensure that the limited data set recipient will only use or disclose the protected health information for limited purposes. This agreement must establish the proposed uses and disclosures of the data and who is permitted to have access to the data, and must ensure that no other use will be made of the data, no attempt will be made to identify or contact individuals whose data are included in the limited data set, and appropriate safeguards are in place to protect the data from unauthorized use.

E. Collection of Identifiable Health Information

The following guidelines for handling identifiable new healthcare information became effective on April 14, 2003: Under the "preparatory to research" provision of the HIPAA Privacy Rule, an investigator may maintain identifying information at the end of the screening conversation until the subject meets with study staff to discuss the study further and sign the consent form. If identifiable health information is collected on persons who are not enrolled, there are two options: (1) destroy the information or (2) if a failure log must be maintained, the PI must obtain authorization from each individual. During this meeting, the subject must be asked to sign the written authorization to use and disclose his/her identifiable healthcare information and be given a copy of the authorization form.

F. Telephone Screening

At the beginning of a phone pre-screening conversation, potential subjects should be informed of the nature and sensitivity of the questions, asked whether this is an appropriate time for them to answer these questions, and told how long the phone call is expected to take. The questionnaires or screening tools that will be used must be submitted to the IRB for review prior to use. A script of what will be said by study staff must also be submitted for review and approval.

The researcher should record only the subject's first name or initials at the beginning of the screening conversation; explain to the subject that s/he will be asked a set of

questions to determine eligibility and that at the end, only if s/he appears to be eligible and is interested in pursuing the study, will s/he be asked to provide contact/identifying information (e.g. last name, address, birth date, Social Security number or hospital medical record number). By following this procedure, **identifiable** healthcare information is only created for those persons who likely meet eligibility criteria. And for those persons who do not meet entry criteria, only **non-identifiable** health information is created. The collection of non-identifiable health information is not subject to privacy regulations. But the collection of identifiable, historical medical information (even by telephone) creates new Protected Health Information (PHI) and obligates the researcher to provide all of the HIPAA Privacy protections.

G. Pre-Screening Through Centralized Phone Banks

National advertisements are sometimes used to recruit subjects for large multi-center studies. Typically, centralized phone banks or operators receive calls from individuals who see such advertisements, and then screen subjects and refer those eligible and interested to local investigators. Phone screeners interacting with potential subjects in this setting are generally not employees or healthcare providers, and typically work from a script or data collection tool that must be reviewed and approved by the IRB before use. Such a recruitment plan should be noted in the protocol, and forwarded to the IRB for review and approval prior to implementation. Research sponsors must comply with HIPAA privacy regulations regarding the use of such a centralized phone bank. Potential subjects should be told they are speaking to a non-medical screener at a centralized phone bank, and not be led to believe they're speaking with a physician or member of the actual clinical research team. This is especially relevant to protocols involving depression or other psychiatric illnesses. Study Sponsors or their screeners should have policies on what will happen if subjects calling are found to be at serious risk of harm to self and others (e.g. suicidal) and provide such plans to the IRB for review. The guidelines listed above may not be applicable to every situation that arises in the research process. Alternative approaches may be considered on a case-by-case basis.

H. Retaining Information Obtained From Pre-Screening

It is acceptable to retain non-identifying information about individuals who are pre-screened for a study, but do not actually pursue the study or enroll. In fact, this is often desirable or even requested by industrial or academic sponsors to obtain information about the entire pool of individuals interested or potentially eligible for the study. Pre-screening sheets from individuals who did not provide identifying information can be retained with no further action. Pre-screening logs with identifying information may also be retained in research files, but must have segments containing identifiable information redacted. If identifiable health information is to be retained, a HIPAA Authorization must be secured from each of the individuals screened.

I. Family Members

If recruitment of family members is planned, for confidentiality reasons, the primary patient should not be asked to provide the name of the family member(s) directly to the investigator. Rather, the subject should be asked to contact family members. If the family member is willing to speak with the investigator, then the family member should be asked to contact the investigator. When research includes family members, the protocol and consent form must indicate how family members will be contacted.

J. Physician-to-Physician Referrals

Investigators may contact other physicians as appropriate to assist in identifying potentially eligible subjects. The other physician can then inform the potential subjects of the study opportunity and provide the investigator's study contact information. To protect patient privacy and maintain confidentiality, the information exchanged about potential subjects between physicians and investigators must comply with HIPAA.

VI. Research on the Protected Health Information of a Decedent

The IRB may permit the use and disclosure of the protected health information of a decedent for research purposes. In order to permit such a use or disclosure, the IRB must obtain representations from the Principal Investigator that the use or disclosure is sought *solely* for research on the protected health information of a decedent (*e.g.*, researchers may not request a decedent's medical history to obtain health information about a decedent's living relative) *and* that the information for which use or disclosure is sought is necessary for the research purposes. Moreover, the Principal Investigator must provide, at the IRB request, documentation of the death of any individuals about whom information is sought.

VII. Consents Obtained Prior to April 14, 2003

In some cases, a researcher will have obtained, before April 14, 2003, some type of express legal permission from an individual identifying a specific ongoing research project that includes treatment of individuals, such as a consent to participate in a clinical trial.

- If the permission *specifically authorizes* a use or disclosure of protected health information for purposes of the research project, the IRB may permit such use or disclosure for purposes of that project.
- If the permission is a *general consent* to participate in the research project and *does not* specifically authorize the use or disclosure of protected health information for purposes of the project, the IRB may permit a use or disclosure for purposes of that project *only* if the hospital is conducting or participating in the research.

Example: A multi-center study begun in May of 2002 involves an examination of the effectiveness of a course of treatment with a cancer drug not yet FDA-approved. The hospital is not a research site. Study events include monthly blood tests that can be performed by any qualified health care professional, whether or not associated with the study. If a subject presents at the hospital after April 14, 2003 seeking a blood test for the research study, the hospital may perform the test and disclose the results to the researchers *only* if the Privacy Officer receives a consent that *specifically authorizes* the blood test and disclosure. The general consent to participate in the trial would not suffice because the hospital is neither conducting nor participating in the research. If a researcher requested that the hospital disclose a subject's protected health information held by the hospital because of its relevance for the subject's enrollment in the trial, the general consent would be inadequate for the same reason. Even a consent specifically authorizing a use or disclosure would be inadequate if the consent applied, by its terms, only to uses and disclosures at a study site.

In either case, the IRB must honor any limitations in the express legal permission.

VIII. De-identified Information

The IRB may allow de-identified information to be used and disclosed for research purposes without restriction. Information may only be considered de-identified when either (1) a qualified statistician documents his or her determination that the risk of identification is very small, or (2) the information meets the requirements described in **Appendix R** of this policy. If the IRB has any doubts as to whether protected health information has been de-identified

within the meaning of this policy, the information should be treated as though it were *not* de-identified and neither used nor disclosed for research purposes without meeting another exception.

IX. Subject Authorization for Research.

The IRB may allow the use and disclosure of protected health information pursuant to a completed and signed Research Authorization form. Permissible uses and disclosures are limited to those described in the authorization, even though those permissible uses and disclosures may be more limited than what the hospital's Notice of Privacy Practices describes. In addition, Investigators and their staff must work with the IRB to limit their uses and disclosures of protected health information to the minimum necessary to accomplish the intended purpose of the use or disclosure, as explained in the hospital's policies on the Minimum Necessary Standard.

The Research Authorization form must be completed by the Principal Investigator for the research subject's review and signature. It is the responsibility of the Principal Investigator to ensure that the Research Authorization form covers the uses and disclosures necessary for the research study.

Upon preparing the form, the Principal Investigator must submit the form to the Privacy Officer for a determination as to whether the requested uses and disclosures will be permitted once the Research Authorization forms are signed by the subjects. The Privacy Officer must sign the Privacy Officer Approval at the bottom of the Research Authorization form before any protected health information obtained by the hospital may be used or disclosed for research purposes. The Privacy Officer's approval should be obtained *before* submitting any protocol to an IRB for review so that the researchers are not later forced to return to the IRB because of modifications to the form requested by the Privacy Officer. Many IRBs will likely *require* such prior approval; researchers should consult the relevant IRB's operations manual for more information.

In addition to the Research Authorization, if medical staff or hospital staff will provide any treatment to subjects on hospital premises in connection with the study, the hospital or the Principal Investigator must collect a signed Individual Consent from every research subject who does not already have one on file at the hospital.

No one may participate in any hospital study without signing the Research Authorization form. Nevertheless, in presenting the Research Authorization form to prospective subjects, researchers should never suggest that failure to sign the form will limit access to any treatment that may be available outside the study. Any questions about the availability of such treatment outside the study should be referred to the prospective subject's physician(s). Any other questions about the Research Authorization form should be directed to the Privacy Officer or to the Privacy Officer's designee who has assessed, or who will assess, the Principal Investigator's request for permission to use or disclose protected health information for research.

X. IRB Approval of Waiver

The IRB may allow the use and disclosure of protected health information for research purposes if the IRB grants a partial or total waiver of the authorization requirement (Request for a Waiver of Consent and Waiver of Authorization under HIPAA - **Appendix H**). If the IRB grants only a *partial waiver* – that is, if it modifies or waives only some elements of the Request for a Waiver of Consent and Waiver of Authorization under HIPAA (**Appendix H**)., the IRB must condition the use and/or disclosure of any protected health information for research purposes on

compliance with any authorization requirements not waived and as modified. For example, if an IRB grants a partial waiver of authorization to allow a researcher to obtain protected health information to recruit potential research participants, the researcher would still have to obtain authorizations from the subjects to use or disclose protected health information for the study itself.

If a Principal Investigator intends to apply to an IRB for a waiver of these authorization requirements, he or she should first present the full IRB application package to the IRB Administrator for a preliminary review that the requested use or disclosure would be applicable The IRB may only grant final approval of any requested uses or disclosures of protected health information for research purposes pursuant to an IRB waiver if the IRB has received appropriate documentation of the waiver, as listed on the Request for a Waiver of Consent and Waiver of Authorization under HIPAA (**Appendix H**).

If the IRB approves only the use or disclosure of *certain information* from individuals' medical records, and not individuals' *entire* medical records, this must be stated on the document certifying IRB approval. The IRB approval document should include a statement that the waiver has been reviewed and approved under either normal or expedited review procedures and that all applicable procedures were followed.

If any such documentation is missing or inadequate, the IRB Administrator will notify the Principal Investigator and any missing/inadequate information can/will hold of the IRB's review.

Note: A waiver of individual authorization under this policy is *not* a waiver of the requirements of informed consent for the project or of any other consent required by the hospital's policies. The IRB may waive or alter informed consent requirements, but the IRB must review a request to waive or alter informed consent requirements *separately* under criteria set forth in the Common Rule.

XI. Individual Access

Individuals generally have a right to access all their protected health information maintained by the hospital or its business associates. All patient requests for access to protected health information obtained in the course of research should be referred to the hospital's Records Department for processing in accordance with the hospital's policy *Patient Access to Protected Health Information*, which provides detailed guidelines for responding to such requests. The Records Department will determine, with assistance from the researcher and the IRB whether access to protected health information may be denied under the exception described in this section of this policy.

Approvals for:
Policy Governing Review and Approval of Human Subject Investigation and Research
(Policy # 8611-072)
Obtained electronically via the Sentact Policy Module

Phyllis August, MD, MPH
Director, Lang Research Center

Pinchi Srinivasan, MD
IRB Chairperson

Tracey Letang
Compliance and Privacy Manager

William Wisseman, Esq.
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Stephen Rimar, MD
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