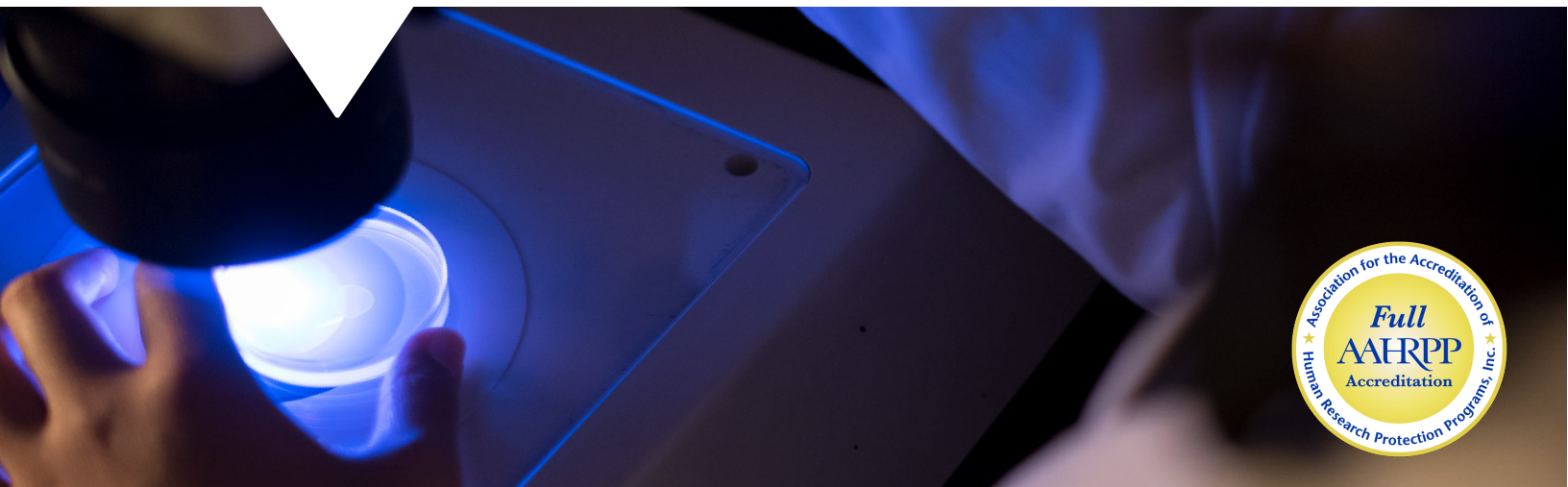
NYU Langone Health

Human Research Protections Policies and Procedures



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1. REVISION HISTORY

Prepared by NYU Langone Health Institutional Review Board (IRB),
Revised:

- *January 31, 2008*
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- *March 15, 2010*
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- *April 7, 2014: changes to 10.6*
- *August 1, 2015: AAHRPP updated requirements made*
- *January 1, 2016: replaced numbering for all chapters/sections*
- *January 21, 2016: included Dept. of Defense language, new section 9.7*
- *May 5, 2016*
- *October 12, 2016: updated section 7.2 to reflect electronic system update*
- *November 28, 2016: minor update to section 15.1 Principal Investigator (staff allowed to be PI)*
- *February 2, 2018: change to definition of Research Team where mentioned, section 10.13 added, 14.6 updated.*
- *April 4, 2018: change to 15.5, UAP reporting time frame, policy adjusted for consistency to match*
- *January 16, 2019: updated to reflect 2018 revisions to Common Rule; expand policy on use of external IRBs for review and oversight of NYU Langone Health research; add sIRB policy where NYUGSoM IRB is acting as single IRB; add policy to require updating of NYU Langone Health employee CVs; editorial changes throughout*
- *May 14, 2020: updated Table of Contents; NYU Winthrop merger-related updates including update to Section 3 "NYU Langone Health" definition to add NYU Long Island School of Medicine; references to Vice Dean for Science revised to reflect delegated authority of NYU Langone Health Chief Scientific Officer; Section 15.1 (Investigator Classifications: Who May Serve as Principal Investigator) updated to incorporate NYU Long Island School of Medicine faculty.*
    - *<u>Additional major changes</u>: Section 5.4 (Single IRB Review) revised to reflect change to Common Rule effective January 19, 2020; updates to procedures in Section 8.8 (Unanticipated Problems); Section 8.10 (Appeal of IRB Decisions) updated to clarify additional appeals process; Section 10.7 (Documentation of Informed Consent – Signed Consent) revised to clarify what is required when short form written consent is used; Section 10.12 (Consent and Language Barriers) revised to provide clarity on documentation requirements, use of interpreters and witnesses in consenting non-English speaking subjects; Section 11.3 update to add requirement on re-consenting subjects upon reaching age of majority; Section 12.1 (Complaints) updated to include external IRB procedures for review of complaints and notification to NYU Langone Health; Section 14.3 (IND/IDE Requirements) and 14.5 (Responsibilities in Research of Investigational Drugs and Devices) updated to reflect current regulations and NYU Langone Health Human Subject Research SOPs; Section 14.6 (Emergency Use) updated to reflect current regulations; Section 15.11 (Conflict of Interest) updated to align with current conflict of interest policies; Section 17.9 (Community Based Research) to include CEPHR program.*
- *September 28, 2020: updates requested by AAHRPP made. Section 5.5 (Roles and Responsibilities) revised to clarify who oversees Office of General Counsel; Section 5.7; Section 5.8; Section 6.7; Section 10.13*
- *May 1, 2021: Incidental Findings; Section 17.10*
- *June 1, 2021: Research Involving Employees and Students as Research Subjects; Section 17.3*
- *February 22, 2022: Institutional Policy on Research with Digital Data Collection Tools, Section 17.11*
- *October 24, 2022: updated Table of Contents; entire policy updated throughout (e.g., changes in titles, processes) to reflect establishment of Human Research Protections (HRP) division; updated throughout to reflect NYU Langone Health IRB Operations oversight of NYU Langone Long Island School of Medicine (formerly Winthrop University Hospital); Reportable New Information, Section 8.8 updated for clarity and consistency with submission procedures; Section 8.11 Sponsored Research Contracts edited to reflect current SPA and OSR Contracts review processes; Quality Improvement & Assurance (QIA) Policy and Procedures added as new Section 15; Section 16.2 Investigator Classifications: Who May Serve as Principal Investigator revised to reflect change in definition of nurses who may serve as PIs; Section 17.3 Applicability of HIPAA on Research: PI responsibilities for use of decedents' Protected Health Information updated.*
- *February 9, 2023: Training and Ongoing Education of Principal Investigator and Research Team, Section 16.8 updated continuing education and recertification requirements for faculty researchers.*
- *May 1, 2023: Section 12.2 Non-Compliance amended to reflect procedure, role of IRB Senior Manager; Section 18.11 Institutional Policy on Research with Digital Data Collection Tools updated to add Survey Tool Technology and Live Two-Way Communication Technology.*
- *September 1, 2023: Section 9.7 Special Requirements for Research Funded by the Department of Defense amended to reflect current DoD requirements (DoD Instruction 3216.02 – appointment of Research Monitor no longer required); Institutional Policy on Managing Disruptive Research Subjects added, Section 10.6 and remainder of section renumbered.*
- *December 11, 2023: Section 2.3, Roles and Responsibilities of IRB Subcommittees; Section 5.4*

- *January 2, 2024: Section 5.4, NYU Langone Health IRB Relationships with Other Institutions added information to clarify the role of External Relations; Section 5.5, NYU Langone Health as Coordinating Center added a new section on the role of HRP when NYU Langone acts as a coordinating center.*
- *March 28, 2024: Section 8.10, Appeals of IRB Decisions re-written to clarify the requirements and process of submitting an appeal.*

2. HUMAN RESEARCH PROTECTIONS

2.1 INTRODUCTION AND MISSION

The *NYU Langone Health Human Research Protections Policies and Procedures* details the policies and regulations governing research with human subjects, and procedures for submitting research proposals for review by the NYU Grossman School of Medicine ("NYUGSoM") and NYU Grossman Long Island School of Medicine ("NYUGLISoM") IRBs (together, the "NYU Langone Health IRBs"). These *Policies and Procedures* apply to all research involving human subjects if NYU Langone Health faculty, staff, students, or facilities are involved, regardless of sponsorship and/or performance site, whether domestic or foreign.

NYU Langone Health fosters a research environment that promotes respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of NYU Langone Health. In the review and conduct of such research, actions by NYU Langone Health will be guided by the principles set forth in the *Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (often referred to as the "*Belmont Report*"). Research will be performed in accordance with the Department of Health and Human Services ("DHHS") policies and regulations at 45 CFR 46 (also known as the "Common Rule"), and the Food and Drug Administration ("FDA") policies and regulations at 21 CFR 50 and 21 CFR 56, as applicable. All of these principles stress such factors as, *inter alia*, respect for persons, beneficence, and justice. NYU Langone Health will also act in conformance with all other applicable federal, state, and local laws and regulations.

In order to effectively conduct human research and protect all research subjects, NYU Langone Health maintains a division of Human Research Protections ("HRP"), which oversees the federally-registered NYU Langone Health Institutional Review Boards ("IRB"), External Relations (overseeing use of external IRBs and Single IRB (sIRB) services), Quality Improvement & Assurance (QIA), Embryonic Stem Cell Oversight Committee, and Research on Decedents Oversight Committee (RDOC). HRP is responsible for ensuring review of research involving human subjects that is conducted by NYU Langone Health, its Schools of Medicine, Centers, and Institutes. HRP also ensures that all personnel involved in such research activities or oversight of such research activities understand and comply with the ethical standards of research, and federal, state, and local laws and policies on experimentation on human subjects.

HRP accomplishes this by strategically bringing together the many various components of human research protections at NYU Langone Health to ensure that all activities involving human subjects are reviewed and managed through the lens of ethical standards and protection of subjects' rights and welfare. HRP's activities are centered on the idea that providing resources to the research community ensures the protection of individuals who participate in NYU Langone Health research projects, and promotes the conduct of high-quality, ethical research. HRP's staff assist investigators and research teams in navigating the complex regulatory landscape.

RESOURCES FOR THE HRP

NYU Langone Health's Chief Scientific Officer or their designees (the Senior Vice President of Clinical Research Operations and Regulatory Affairs), the IO, and the Vice President of Internal Audit, Compliance & Enterprise Risk Management provide resources to the HRP. The Chief Scientific Officer and/or their designees oversee:

- the NYU Langone Health IRBs and IRB Operations;
- Sponsored Programs Administration (SPA);
- the Clinical Research Support Unit (CRSU);
- OSR Contracts;
- Regulatory Affairs and Business Operations (RABO); and
- other business units comprising the Office of Science and Research.

The Vice President of Internal Audit, Compliance & Enterprise Risk Management ("IACERM") oversees the Office of Research Compliance.

Resources include adequate meeting and office space, and staff for conducting HRP business. Office equipment and supplies, such as technical support, file cabinets, computers, internet access, and copy machines (etc.) will be made available to the IRB and IRB Operations staff. In addition, the Chief Scientific Officer and Vice President of IACERM will discuss resource needs with other business units related to the HRP, such as the Office of General Counsel.

On an annual basis, the Senior Director, HRP will review the activity, workload and resources (including personnel) of the IRB and IRB Operations, and will make a recommendation with regard to resources to the Chief Scientific Officer and the IO. The resources provided for the IRB and IRB Operations will be reviewed during the NYU Langone Health annual budget review process.

2.2 ETHICAL PRINCIPLES: THE BELMONT REPORT

HRP's review and oversight of research involving human subjects must follow the three principles set forth in the *Belmont Report*:

- that voluntary participation by the subjects, indicated by free and informed consent, is assured;
- that an appropriate balance exists between the potential benefits of the research to the subject or to society and the risks assumed by the subject; and
- that there are fair procedures and outcomes in the selection of research subjects.

These principles are referred to as "Respect for Persons, Beneficence, and Justice", and are the touchstones of ethical research.

RESPECT FOR PERSONS: VOLUNTARY PARTICIPATION AND INFORMED CONSENT

One of the most important elements in any research involving human research subjects is the assurance of voluntary informed consent. Any person who may become a research subject, whether designed for his/her/their own direct benefit or for the advancement of scientific knowledge in general, must understand as completely as possible what the study entails and the potential risks and benefits of the study. The person must give his/her/their consent freely, without pressure or inappropriate inducement. The NYU Langone Health IRBs strive to ensure voluntary informed consent of research subjects through a careful review of the recruitment and consent process, and a further review of the details of the consent form and/or any other materials to be viewed by subjects.

The informed consent concept is further extended to those studies in which the subjects are not able to give personal consent for themselves. In this situation, the consent document is addressed to those who have been designated responsible for the research subject's wellbeing (e.g., parent of a child). The IRB's concern is to verify that the consent process and document are likely to assist these persons in making an informed

decision as to the best interests of the research subject. The capacity for truly informed and voluntary participation in research varies widely among study populations. At one extreme, there may be ample understanding and manifest freedom from coercion; at the other, there may be degrees of understanding and freedom that affect the consent of potential subjects. The IRB must exercise special care when considering subjects whose ability to give free and informed consent may be compromised in any way.

BENEFICENCE: THE RISK-BENEFIT RATIO

For any proposed activity that falls under its jurisdiction, the IRB is charged with deciding whether:

> "The risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept (those) risks."
>
> *(Federal Register, May 30, 1974)*

There are risks of injury or discomfort to the individual that can be physical, psychological, financial, and/ or social. Conversely, there may be potential benefits to the individual, to a group to which the individual belongs, and/or to society. In its review of applications, the IRB must carefully assess the types and degrees of both risks and benefits for a given subject population, as well as the communication of these risks and benefits to the subject in the consent process and informed consent form. While the IRB is not charged with reviewing scientific design *per se*, it must occasionally do so in order to assess the risk/benefit ratio. If a study design seems inadequate in attainment of the stated aim of the investigation, then no benefit can be anticipated from conducting the study. Thus, there would be no justification for placing any research subject at risk, however minimal. Therefore, the design of the study must be sound, and the nature and likelihood of all risks and benefits must be made clear in any application to the IRB.

JUSTICE: THE FAIR SELECTION OF RESEARCH SUBJECTS

Both the risks and the potential benefits of research should be spread fairly among potential research subjects and research subject groups. Study design and selection of subjects should avoid bias for or against particular group based on such factors as gender, sexual orientation, socioeconomic status, immigration status, race, or social group.

SHARING RESEARCH RISKS

The guiding principle in the ethical selection of research subject groups is that any risks of the research should fall upon the groups who might benefit from the research. If the results of a risky protocol might benefit the general population, it would be unethical to focus subject recruitment on vulnerable or disadvantaged groups (e.g., institutionalized people or prisoners; patients at free clinics primarily patronized by people unable to afford other medical care) simply because this population is easily accessible or can be persuaded to participate.

Further, an undue share of research risks should not burden groups already burdened by other factors. Rather, attempts should be made to include a fair sampling of the populations who might benefit from the study. When research involves persons whose autonomy is compromised, it is expected that the research bear some direct relationship to the conditions or circumstances of the research subject population. In addition, groups fully able to consider the research risks and informed consent process should be considered for selection in a study prior to involvement of the more vulnerable populations. For example, investigational

drugs are typically tested in adults prior to being tested in children. Certain investigational drugs and procedures may be tested in healthy volunteers prior to being tested in patients.

SHARING RESEARCH BENEFITS

Attention has increasingly been paid to the rights of various groups to be included in research. Through advocacy groups, many patients have come to insist on having access to experimental treatments, because these treatments may potentially provide the best medical care available. In addition, researchers, ethicists and public officials have recognized that because many clinical trials focus primarily on white middle-class research subject groups, the results of certain trials were of questionable value for members of other social, racial, sexual, and ethnic groups. As a result, both the National Institutes of Health ("NIH") and the FDA now require that a study design include as broad a range of research subjects as feasible, and further that the data be analyzed to uncover responses that differ between groups. For example, where women of child-bearing potential, pregnant and nursing women were previously routinely excluded from new drug trials, it is now required that, whenever possible, these women be asked to make their own choices after being fully informed of the risks of the research.

2.3 ROLES AND RESPONSIBILITIES

INSTITUTIONAL OFFICIAL (IO)

The IO is ultimately responsible for oversight over the NYU Langone Health HRP and the IRBs, and the conduct of research at or under the auspices of NYU Langone Health in compliance with institutional policies and all applicable regulations for the protection of human subjects. The IO is responsible for ensuring NYU Langone Health's HRP, the IRBs and NYU Langone Health IRB Operations ("IRB Operations") have the resources and support necessary to for the IRBs to comply with all federal regulations and guidelines governing human subjects research, and with institutional policies. The IO is responsible for ensuring that legal counsel is available to the IRB for guidance, or for seeking legal and regulatory guidance where needed, to support human research protections. The IO or the IO Designee (Senior Director, HRP) signs all assurances regarding human subjects research to governmental oversight agencies.

SENIOR DIRECTOR HRP

The Senior Director of HRP reports to the Senior Vice President, Clinical Research Operations and Regulatory Affairs, and is responsible for providing strategic vision and oversight of NYU Langone Health's integrated HRP program. The Senior Director of HRP ensures that all core components of HRP across the institution work collaboratively in efforts to protect human participants in NYU Langone Health research. The Senior Director is also responsible for the efficient management, oversight, and administration of operations in the following HRP units: Institutional Review Board (IRB), External IRB and Single IRB, Scientific Review Committee (SRC), Embryonic Stem Cell Research Oversight (ESCRO) and Research on Decedents Oversight Committee (RDOC).

The Senior Director is a voting member of the IRB.

INSTITUTIONAL REVIEW BOARD ("IRB")

NYU Langone Health's IRBs, and other IRBs to which NYU Langone Health cede IRB review responsibilities under reliance agreements, are administrative bodies established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of NYU Langone Health. These Boards prospectively review and make decisions concerning all human subjects research conducted at or under the auspices of NYU Langone Health by its employees or agents and/or

research under the IRB's jurisdiction. The IRB discharges this duty by complying with all applicable requirements of federal law, its FWA, and institutional policies.

The NYUGSoM and NYUGLISoM IRBs are managed operationally under NYU Langone Health's IRB Operations. More information about the NYU Langone Health IRBs can be found under Section 5, Institutional Review Boards.

OFFICE OF GENERAL COUNSEL

HRP and the IRB rely on the counsel of NYU Langone Health's Office of General Counsel for the interpretation of applicable law in the jurisdiction(s) where the research is conducted. When there are any questions about conflicting legal requirements, the Office of General Counsel will determine the appropriate resolution. NYU Langone Health's Senior Vice President and Chief General Counsel oversees the Office of General Counsel. The Office of General Counsel also oversees the Conflict of Interest Management Unit (CIMU) which is responsible for handling conflicts of interest for the institution related to research.

IRB CHAIRS

NYU Langone Health's Chief Scientific Officer, in coordination with the IO and the Senior Director of HRP, will appoint a Chair and Vice Chair of each IRB to serve for renewable three-year terms. Any change in appointment, including reappointment or removal, requires written notification.

The IRB Chairs should be highly respected individuals at NYU Langone Health who are fully capable of managing the IRB and the matters brought before it with fairness and impartiality. Moreover, the IRB Chairs must endeavor to be immune to pressure from the institution's administration, the investigators whose protocols are brought before him/her/them, and other professional and nonprofessional sources.

The IRB Chairs are responsible for conducting convened IRB meetings.

The IRB Chairs may designate other IRB members (including but not limited to the Vice Chair or Senior Director of HRP) to perform duties, as appropriate, for review, signature authority, and other functions of the IRB Chairs.

The IRB Chairs will advise the IO and the Senior Director of HRP about IRB member performance and competence.

VICE CHAIRS OF THE IRB

A Vice Chair serves as the Chair of the IRB in the absence of the Chair, and maintains the same qualifications, authority, and duties as the IRB Chair.

SUBCOMMITTEES OF THE IRB

The IRB Chairs, in coordination with the Senior Director, HRP, may establish subcommittees consisting of one or more IRB members.

Duties of an IRB subcommittee may include the following:

1. Serve as designees by an IRB Chair for the expedited review of new or continuing studies, and/or modifications of continuing approved studies and reportable new information. The subcommittee must be experienced (in terms of seniority on the IRB), and must be matched as closely as possible with their field of expertise to the study.
2. Review and approve revisions of protocols previously given provisional approval ("Conditional Approval") by the convened IRB. *See* Possible Actions Taken By IRB Vote.

3. Conduct an inquiry into allegations of non-compliance. The subcommittee may be given a charge by the IRB, which can include any or all of the following:
    - review of protocol(s) in question;
    - review of FDA audit report of the investigator, if appropriate;
    - review of any relevant documentation, including, *inter alia*, consent documents, case report forms, and a subject's investigational and/ or medical files, as the documentation relates to the investigator's execution of her/his/their study involving human subjects;
    - interview of appropriate personnel if necessary;
    - preparation of either a written or oral report of the findings, which is presented to the full IRB at its next meeting; or
    - recommend actions if appropriate.
4. Conduct on-site review of a study. Determination of the review interval and the need for additional supervision and/or participation is made by the IRB on a protocol-by-protocol basis. For example, an on-site review by an IRB subcommittee might occur in a particularly risky research study, or approval might be subject to an audit of study performance where an investigator recently had a protocol suspended by the IRB due to regulatory concerns.

THE PRINCIPAL INVESTIGATOR

The Principal Investigator is the chief protector of the human subjects who participate in his/her/their research, and is ultimately responsible for all research conducted under his/her/their oversight. The Principal Investigator is expected to abide by the highest ethical standards and for developing a protocol that incorporates the principles of the Belmont Report. The Principal Investigator is expected to conduct research in accordance with the approved research protocol and to oversee all aspects of the research by providing appropriate training and supervision of study staff, including but not limited to oversight of the informed consent process.

The Principal Investigator must establish and maintain an open line of communication with all research subjects within his/her/their responsibility. In addition to complying with all the policies and standards of the governing regulatory bodies, the Principal Investigator must comply with applicable institutional and administrative requirements, including but not limited to that of the IRB, for conducting research. The Principal Investigator is responsible for ensuring that all of his/her research staff completes appropriate training and must obtain all required approvals prior to initiating the research. When investigational drugs or devices are used, the Principal Investigator is responsible for providing written procedures for their storage, security, dispensing and disposal.

The Principal Investigator must be qualified, licensed and credentialed for all aspects of the research under his or her oversight, or otherwise delegate such responsibilities to a member of the study team with the requisite qualifications, licenses or credentials. The IRB shall require a licensed physician to be on the study team for any human subjects research requiring a medical intervention.

More information can be found in Section 16, Principal Investigator Responsibilities.

DEPARTMENT CHAIRS

At NYUGSoM and NYUGLISoM, the chairperson(s) of the department administering the research is responsible for ensuring that the Principal Investigator is qualified by training and experience to conduct the proposed research. In addition, department chairs are responsible for ensuring that the Principal Investigator has sufficient resources and facilities to conduct the proposed research.

For each protocol submitted to the IRB for approval, the department chair must certify that he/she/they accept responsibility for assuring adherence to the federal, state, and local regulations and institutional

policies governing the protection of human subjects of research, including applicable institutional credentialing requirements.

Department chairs are required to review all research proposals before they are submitted to the IRB for review. By signing the IRB application, the department chair indicates that they find the study to be scientifically sound, that the study can reasonably be expected to answer the proposed question, and that the department will commit resources required to conduct the research in a way that will protect the rights and welfare of subjects. Such resources include but are not necessarily limited to personnel, space, equipment and time.

OTHER COMPONENTS OF THE NYU LANGONE HEALTH HUMAN RESEARCH PROTECTIONS (HRP)

OFFICE OF SCIENCE AND RESEARCH CONTRACTS (OSR CONTRACTS)

OSR Contracts staff members review and negotiate all agreements with federal, foundation, and non-profit funding sponsors for research, and with industry sponsors for clinical research. This institutional review ensures that all terms of the award are in compliance with institutional policies. Designated senior individuals within OSR Contracts have the authority to execute research agreements on behalf of the institution.

When a NYUGSoM or NYU LISoM grant or contract agreement includes human research activities that will be conducted by investigators who are not employees or agents of NYU Langone Health, a subcontract is executed with the collaborating institution/third party. The subcontract includes the requirement for the collaborating institution/third party to assure compliance with federal regulations for the protection of human subjects in research and to provide documentation of current and ongoing IRB approval for its site upon request. The collaborating institution/third party must also ensure that its key personnel involved in human subjects research are in compliance with the NIH policy on education in the protection of human research subjects and provide documentation of education of its key personnel to the site's IRB.

SPONSORED PROGRAMS ADMINISTRATION (SPA)

SPA staff members review grant proposals submitted to federal, foundation, or non-profit funding sponsors. This institutional review is to ensure completion and compliance with applicable laws, guidelines and institutional policies. Designated senior individuals within SPA have the authority to approve research proposals and to related terms and conditions on behalf of the institution. As a further control, internal documents retained by SPA as part of the application process for extramural funding include Grant applications, Principal Investigator Certification, as well as all ancillary documentation required to support submissions.

CLINICAL RESEARCH SUPPORT UNIT (CRSU)

NYU Langone Health's CRSU provides administrative services related to clinical research supported by commercial entities, including but not limited to clinical trials of new pharmaceutical and medical devices. These include industry-initiated and investigator-initiated studies. The CRSU helps prepare and develop budgets for clinical research agreements contemplating industry support (funding and/or product support), and engages in business development. The CRSU is also responsible for clinical research billing compliance and provides support in the administration of the NYU Langone Health's research billing compliance program.

TECHNOLOGY OPPORTUNITIES AND VENTURES (TOV)

NYU's Technology Opportunities and Ventures (TOV) is responsible for technology transfer activities at NYU including NYU Langone Health. TOV secures patent and/or other intellectual property protection for

commercially-promising discoveries, licenses NYU technologies to existing companies, and facilitates the creation of new companies so that NYU technologies can be developed into products to benefit the public, while providing a return to NYU to support its research and education missions. TOV negotiates agreements with industry to support research at NYU (other than clinical research), and negotiates other research-related agreements including material transfer agreements, inter-institutional agreements, and confidential disclosure agreements.

PROTOCOL REVIEW AND MONITORING COMMITTEE (PRMC)

The PRMC of the NYU Langone Health Perlmutter Cancer Center provides the mechanism for assessing the scientific merit of new oncology trials proposed to be conducted at NYU Langone Health, and the authority to close trials that are not meeting accrual. After being approved by Disease Management Groups and assigned priority scores, all new clinical research protocols are submitted to the PRMC. The PRMC coordinates the submissions for the Bio Statistical Group and coordinates the peer review of protocols for approvals, which are required before the protocol is submitted to the IRB.

OFFICE OF RESEARCH COMPLIANCE

The Office of Research Compliance provides oversight of NYU Langone Health research programs, activities, and processes, in a manner that is independent of HRP. The Office of Research Compliance is responsible for coordinating and monitoring the compliance program to ensure that NYU Langone Health is compliant with federal, state, and local laws and regulations, and with applicable institutional policies.

REGULATORY AFFAIRS AND BUSINESS OPERATIONS (RABO)

RABO assists researchers in complying with requirements for clinical trial registration and results reporting, and regulations applicable to investigators who hold their own INDs or IDEs for the study of drugs or devices that are not approved by the FDA.

NYC HEALTH + HOSPITALS/BELLEVUE RESEARCH REVIEW COMMITTEE (BRRC)

NYC Health + Hospitals/Bellevue's Research Review Committee (BRRC) is responsible for protecting the basic rights, health, and welfare of Bellevue patients and employees who voluntarily consent to participate in research studies. In addition, the Bellevue Research Department staff is responsible for educating potential researchers on the protocol submission and approval process, and for assuring that individuals involved in conducting research-related activities at Bellevue are in compliance with hospital and corporate policies and procedures, as well as federal, state, and city regulations.

The BRRC is chaired by the Chair of the Research Committee of the Medical Board and is comprised of a general medical reviewer, and reviewers from its departments of Psychiatry, Pharmacy, Drug & Formulary, Radiology, Pathology, Finance, the Medical Board, and Executive Administration. BRRC committee members are charged with reviewing protocols, focusing on his/her/their respective area of expertise, and approving them as appropriate in the NYC Health + Hospitals electronic research application system, System to Track and Approve Research ("STAR").

The BRRC is designated as an ancillary research review committee and not an IRB. The BRRC accepts the review and determination by NYU Langone Health IRB's (or their duly authorized IRB of record) for all NYU Langone Health research protocols that will involve human subjects recruited at Bellevue. Once a research study has been granted both NYU Langone Health IRB and BRRC approval, it must obtain final approval from the New York City Health and Hospitals Corporation Research Review Committee, which functions within the NYC Health and Hospitals Research Administration Office. It is through this multi-level approval process that the Bellevue Research Department can ensure that the basic rights, health, and well-being of its research subjects are adequately protected.

NYU LANGONE HEALTH INVESTIGATIONAL PHARMACY

A pharmacist from the NYU Langone Health Investigational Pharmacy serves on the IRB, allowing the NYU Langone Health Pharmacy to have complete information about all IRB-approved research that takes place at the institution and under its jurisdiction. The pharmacist member assures that information about all studies involving drugs used in research is shared with both the Pharmacy staff as appropriate, and that the Investigational Pharmacy is made aware of IRB-approved research involving drugs.

The NYU Langone Health Investigational Pharmacy typically does not engage in the ordering/providing, dispensing, or compounding of drugs used in research, unless the drug is a controlled substance. If a controlled substance, the item is ordered/received by the Investigational Pharmacy and re-issued in appropriate quantities to researchers for animal studies, or, for human studies, pursuant to a study-specific and patient-specific medication order developed by the Investigational Pharmacy in collaboration with the researcher. The manufacture/compounding of drug products that are not commercially available is coordinated by the Investigational Pharmacy with outside pharmacy vendors. However, insofar as inpatient drug studies and/or those outpatient drug studies that have subjects who become inpatients at NYU Langone Health, the Investigational Pharmacy coordinates the use of the study drug while the subject is an inpatient, and all such inpatient study drugs must be provided through the Investigational Pharmacy.

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

NYU LANGONE HEALTH INSTITUTIONAL BIOSAFETY COMMITTEE (IBC)

All research that involves Recombinant or Synthetic Nucleic Acid Molecules ("rDNA") molecules must be in compliance with the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* ("NIH Guidelines"). The NIH Guidelines set forth principles and standards for safe and ethical conduct of research involving rDNA and apply to both basic and clinical research studies.

The NYU Langone Health Institutional Biosafety Committee (IBC) is responsible for approving risk assessment and the biosafety containment levels, assessing the safety of such experiments which occur throughout NYU Langone Health. Principal Investigators must comply with the IBC guidelines and procedures, applicable regulations and guidelines, and all conditions approved by the ICB with respect to their proposed research. For more information, see the *NYU Langone Health Institutional Biosafety Policy*.

3. DEFINITIONS

When the NYU Langone Health IRBs review research that is subject to the 2018 revised Common Rule (date of compliance effective date January 21, 2019) to make Exempt research determinations and evaluations regarding whether a proposed activity constitutes human subjects research when the research (or activity) is conducted or supported by an agency subject to the Common Rule, the definitions identified as "2018 Common Rule" will be applied. Likewise, the revised definitions will be applied, as applicable, to the conduct of the research, investigator responsibilities, and institutional responsibilities. Some of the below definitions were not changed in the pre-2018 Common Rule, but are included here for context.

AGENT

means all individuals performing institutionally-designated activities or exercising institutionally-delegated authority or responsibility.

CERTIFICATION

refers to the official notification by an institution to the sponsoring federal department or agency component, in accordance with the requirements of this Policy, that a research project or activity involving human subjects has been reviewed and approved by an IRB in accordance with an approved assurance.

CLINICAL TRIAL

means a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

COMMON RULE

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

HUMAN SUBJECTS RESEARCH

for the purposes of this Policy is defined as any activity that either

is "research" and involves "human subjects" as those terms are defined by DHHS regulations (45 CFR 46.102); or

is a "clinical investigation" and involves "human subjects" as those terms are defined by FDA regulations (21 CFR 50 and 21 CFR 56).

HUMAN SUBJECT

As defined by DHHS regulations:

[pre-2018 Common Rule] A living individual about whom an investigator (whether professional or student) conducting research obtains:

(1) data through intervention* or interaction** with the individual, or

(2) identifiable**** private information***.

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

[2018 Common Rule] A living individual about whom an investigator (whether professional or student) conducting research:

Obtains information or biospecimens through intervention* or interaction** with the individual, and uses, studies, or analyze the information or biospecimens; or

Obtains, uses, studies, analyzes, or generates Identifiable**** private information*** or *****identifiable biospecimens.

*_Intervention_ includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

**Interaction includes communication or interpersonal contact between investigator and subject.

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

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

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

"HUMAN SUBJECT" as defined by FDA regulations:
An individual who is or becomes a subject in research, either a recipient of the test article or as a control. A subject may be either a healthy human or a patient. In the case of medical device research, a human subject is also means a human on whose specimen an investigational device is used.

RESEARCH

As defined by DHHS regulations:
Is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this regulation, the following activities are deemed NOT to be research:

(1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

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

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

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

"**Generalizable knowledge**" means that (1) conclusions are drawn from particular instances and (2) the information from the investigation is to be disseminated. A "systematic investigation" is defined as a methodical planned inquiry to obtain or ascertain facts.

Activities that meet this definition of "research" may be funded or unfunded, or may be conducted as a component of another program not usually considered research. For example, demonstration and service programs may include evaluation components, which constitute research activities under this definition.

As defined by FDA regulations:
Any experiment that involves a Test Article and one or more human subjects and that either (1) is subject to requirements for prior submission to the FDA under Section 505(i) or 520(g) of the Federal Food, Drug and Cosmetic Act (the "Act"), or (2) is not subject to requirements for prior submission to the Food and Drug Administration under these Sections of the Act, but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit. An experiment, as defined in 21 CFR 312, includes any use of a drug other than the use of a marketed (approved) drug in the course of medical practice, and as defined in 21 CFR 812, includes any activity that evaluates the safety or effectiveness of a medical device. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. [21 CFR 50.3(c), 21 CFR 56.102(c)]

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

Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act" means any activity that evaluates the safety or effectiveness of a device. [21 CFR 812.2(a)] Any activity in which results are being submitted to or held for inspection by FDA as part of an application for a research or marketing permit is considered to be FDA-regulated research. [21 CFR 50.3(c), 21 CFR 56.102(c)]

ENGAGEMENT

Institutions are considered "engaged" in a research project when the involvement of their employees or agents in that project includes any of the following:

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

IRB APPROVAL

refers to the determination of the IRB that the research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other applicable institutional and legal requirements.

MINIMAL RISK (IN CONTEXT OF RESEARCH NOT INVOLVING PRISONERS)

means risk for which the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. [45 CFR 46.404]

NYU LANGONE HEALTH

includes NYU Langone Health System, NYU Langone Hospitals (including all inpatient and ambulatory facilities), NYU Grossman School of Medicine, NYU Grossman Long Island School of Medicine, and all entities that are controlled by any of them, except where specifically excluded.

RESEARCH UNDER THE AUSPICES OF NYU LANGONE HEALTH

means research that is conducted at NYU Langone Health, conducted by or under the direction of any employee or agent of NYU Langone Health (including students) in connection with his/her/their institutional responsibilities, conducted by or under the direction of any employee or agent of the institution using any property or facility of the institution, or involving the use of the institution's non-public information to identify or contact human subjects.

RESEARCH TEAM

for human subjects research and purposes of this Policy, consists of the Principal Investigator and other individuals (also known as "Key Personnel") who contribute to the scientific development or execution of a study in a substantive, measurable way, whether or not they receive salaries or compensation under the applicable protocol, subaward, or contract. The Research Team also consists of individuals who interact directly with human subjects (and/or identifiable information and biological specimens) for research activities including the consent process, analysis and reporting of research data, and research data entry. Individuals on the Research Team must be approved by the IRB and listed on the study's delegation of authority log.

NON-RESEARCH TEAM, OR RESEARCH SERVICE PROVIDERS

for purposes of this Policy, are individuals who perform ancillary services, routine care, non-investigational testing, or other support services for a research study and do not contribute to or have involvement with the scientific development, conduct, execution, analysis or reporting of a study. Individuals with such roles are generally not considered to be members of the Research Team. Non-Research Team individuals do not require IRB approval, but should be added to the delegation of authority log.

TEST ARTICLE

Test articles covered under the FDA regulations include:

- **Human Drugs**
  http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm
- **Medical Devices**
  https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051521.htm
- **Biological Products**
  http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm
- **Food Additives**
  Any substance added to food. Legally, the term refers to "any substance the intended use of which results or may reasonably be expected to result – directly or indirectly – in its becoming a component or otherwise affecting the characteristics of any food." This definition includes any

substance used in the production, processing, treatment, packaging, transportation or storage of food.

- **Color Additives**
  Any dye, pigment or substance which when added or applied to a food, drug or cosmetic, or to the human body, is capable (alone or through reactions with other substances) of imparting color.
  https://www.fda.gov/Food/IngredientsPackagingLabeling/ucm112642.htm
- **Foods**
  Includes dietary supplements that bear a nutrient content claim or a health claim.
- **Infant Formulas**

4. INSTITUTIONAL AUTHORITY

NYU Langone Health's HRP operates under the authority of this Policy. The operating procedures in this Policy govern the HRP, QIA, the conduct of the NYU Langone Health IRBs and their review of all Human Subjects Research conducted under the auspices of NYU Langone Health, as well as that of any other duly authorized institutional review board in accordance with this Policy, including duly authorized external IRBs and single IRBs. This Policy is made available to all investigators and research staff by being posted on the NYU Langone Health's Human Research Protections website.

NYU Langone Health's Chief Scientific Officer designates the individual who serves as the IO for the purpose of carrying out NYU Langone Health's HRP. Further, the Chief Scientific Officer or designee identifies, as necessary, other individuals to whom responsibility is delegated for administrative oversight of the individual components of the HRP.

The Senior Director of HRP is the designated HRP leader, provides oversight for the HRP, and exercises operational responsibility, on a day-to-day basis, for the institution's program for protecting human research subjects.

The NYU Langone Health IRBs, working with the IO, are administrative bodies designated to protect the rights and welfare of human research subjects participating in research activities conducted under the auspices of NYU Langone Health and have jurisdiction over all Human Subjects Research conducted under the auspices of the institution.

All Human Subjects Research conducted at the following NYU Langone Health facilities or components are considered research activity of NYU Langone Health and are subject to these Policies:

- NYUGSoM and NYUGLISoM including all institutes and faculty group practices thereunder; and
- all hospitals within the NYU Langone Hospitals, including Tisch Hospital, NYU Langone's Hospital for Joint Diseases, NYU Langone Hospital - Long Island, and NYU Langone Hospital – Brooklyn.

NYU Langone Health's IRB may also oversee certain human subjects research at other affiliated institutions in accordance with IRB authorization agreements, including NYU College of Dentistry and NYU Rory Meyers College of Nursing, NYU Family Health Centers at NYU Langone, NYC Health + Hospitals/Bellevue, and the Department of Veteran's Affairs New York Harbor Healthcare System.

Unaffiliated institutions with whom NYU Langone Health enters into an IRB reliance agreement (such as those for which NYU Langone Health's IRB acts as a single IRB) are also subject to the Policies of the NYU Langone Health IRBs.

4.1. ASSURANCE OF COMPLIANCE

The FWA is an assurance of compliance with the federal regulations for the protection of human subjects in federally-funded research. NYUGSoM holds a federal-wide assurance, ("FWA") 00004952. NYUGLISoM's FWA is 00000726. The FWA is approved by the HHS Office of Human Research Protections ("OHRP"), thereby permitting other departments and agencies that have adopted the Federal Policy for the Protection of Human Subjects to rely upon the FWA for the research that they conduct or support. Under this Policy, NYU Langone Health maintains these same standards for all Human Subjects Research regardless of funding status.

4.2. REGULATORY COMPLIANCE

The NYU Langone Health IRBs and any other IRB to which NYU Langone Health cedes IRB review for its research are responsible for ensuring compliance with institutional policies and applicable federal law in its review and oversight of Human Subjects Research. This is done through carrying out the IRB review processes as set forth in this Policy, education, and quality assurance review programs conducted by the NYU Langone Health Human Research Protection Quality Improvement & Assurance (QIA) Division staff, among other things. All Human Subjects Research under the auspices of NYU Langone Health must be conducted in accordance with this Policy, the Common Rule, 21 CFR 50 and 56 (as applicable), and applicable state and local law in the jurisdiction where the research is conducted.

The NYU Langone Health IRBs voluntarily apply the International Conference on Harmonization ("ICH") Good Clinical Practices ("GCP") Guidelines, sometimes referred to as "ICH-GCP" or "E6", only to the extent that they are compatible with FDA and DHHS regulations.

4.3 CONDUCT OF QUALITY ASSURANCE AND QUALITY IMPROVEMENT INITIATIVES (QII) FOR HRP

NYU Langone Health is committed to ensuring research involving human subjects is conducted in compliance with the ethical principles outlined in The Belmont Report and all federal, state, and local regulations governing human research. The quality assurance methods whereby the HRP processes are reviewed and tracked internally are described in greater detail below in NYU Langone Health IRB HRP Quality Improvement Initiatives, referred to here as "**QII**." The goal of the QII is to help fulfill NYU Langone Health's responsibility for ensuring compliance with applicable regulations, and to promote an environment in which Human Subjects Research will be conducted according to the highest standards. Implementation of the QII at NYU Langone Health serves to evaluate HRP at varying levels, increase awareness among all NYU Langone Health research staff and faculty of existing processes, operating procedures, and educational programs, and to gather information necessary for enhancing protections.

COMPONENTS OF HRP QUALITY IMPROVEMENT INITIATIVES (QII)

The QII consists of four main areas of the HRP process, and focuses on the study, the researchers, and/or the IRB records maintained by IRB Operations. They are: (1) study start-up support, (2) study ongoing support, (3) HRP educational programs, and (4) performance metrics.

STUDY START-UP SUPPORT

IRB Submission Assistance

To facilitate the IRB review and approval process for both initial and continuing review submissions, IRB Operations offers investigators assistance with their IRB submissions through the IRB Outreach Program. This service includes reviewing and providing feedback on protocol and informed consent documents, answering questions regarding submission requirements, navigating forms, and identifying questions/concerns that reviewers may potentially raise. IRB Managers will also use this opportunity to provide investigators and study staff with practical tools and other relevant recommendations for improving study site compliance and performance. Investigators are encouraged to contact the IRB Operations for assistance with submissions.

Study Site Initiated Review

Comprehensive on-site reviews are conducted at the request of study teams. A Principal Investigator or a member of the research team can request an on-site review by the QIA Division to ensure overall compliance, to address a specific issue and/or to help prepare for internal inspection.

Consultation for Study Start-Up

The QIA Division can assist investigators with "study start-up" for researcher-held investigational drug and device studies. Using the IRB-approved protocol, and working with the research team, the QIA Division staff can develop study-specific data collection forms to allow for the capture, access, and management of study data. In addition, QIA Division staff can offer assistance with study coordination, including proper record keeping, and study documentation.

STUDY ONGOING SUPPORT

Routine Reviews

Routine Reviews (as defined in Section 15) are conducted internally to assess the Principal Investigator's compliance with federal, State, and local laws, NYU Langone Health HRP and IRB policies, identify areas for improvement, and suggest recommendations based on existing policies and procedures. Routine Reviews are carried out by the staff of the QIA Division in compliance with this Policy.

Preparation for External Audit

The QIA Division staff assists study sites as they prepare for audits/inspections by the FDA, NIH, or other external agencies. Upon receipt of an audit notification, a Principal Investigator may request an on-site review of all study files. This internal pre-audit provides the Principal Investigator/study team the opportunity to identify deficiencies, and take necessary corrective actions before an external audit commences.

HRP EDUCATIONAL PROGRAMS

NYU Langone Health's HRP educational programs are designed for investigators, their research staff, and IRB members and staff based on the results of the QII reviews. *See also* this Policy, Training/Ongoing Education of Chair and IRB Members in Regulations, Procedure; and Training & Ongoing Education of Principal Investigator and Research Team.

For Investigators and their Research Staff

There are regularly scheduled educational sessions which focus on Principal Investigators and study team responsibilities in accordance with the ICH Guidelines for Good Clinical Practice. These include the Clinical Research Foundational Program (2 day course) and the Principal Investigator Development and Resources course (PINDAR). Sessions include those that cover IRB-specific requirements for all submission types in accordance with institutional policies and OHRP/FDA regulations. The IRB can require completion of any of these sessions as part of a corrective action plan following an audit.

- Clinical Research Foundational Program

Offered both live and virtual, this 2 day mandatory program targets the clinical research workforce at the point of onboarding. This program is required learning and is TransCelerate-recognized.

- Principal Investigator Development and Resources (PINDAR)

A live, in-person, six hour class for Principal Investigators: There are no "tests" or assessments for this program.

Additionally, custom in-service sessions are required for study teams upon the IRB's confirmation of serious non-compliance. These sessions are designed to address specific issues of non-compliance revealed during an audit conducted by the QIA Division, and are scheduled after the study team has received an official communication regarding serious non-compliance.

IRB Board Members and IRB Operations Staff

Initial and ongoing education required and available for IRB Board members and IRB Operations staff is described in this Policy, Training/Ongoing Education of Chair and IRB Members in Regulations, Procedures (See Section 6.7 for detailed information). IRB Operations staff receive ongoing training to address issues as they are identified.

Internal IRB Compliance Reviews

Internal compliance reviews are conducted by HRP staff. These reviews are designed to assess compliance with local, State, and federal laws, NYU Langone Health IRB and HRP policies and procedures, and to improve current IRB operations. The results of the reviews will be reported to the Senior Director, HRP and IRB.

The internal compliance reviews conducted by the HRP staff may include but are not limited to the following:

- Review of IRB meeting minutes to determine that adequate documentation of the meeting discussion has occurred. This will include assessing documentation related to discussions for protection of vulnerable populations as well as other risk/benefit ratio and consent issues that are included in the criteria for IRB approval;
- Assessment of IRB meeting minutes to assure that quorum was met and maintained;
- Assessment of current adverse event reporting processes;
- Assessment on whether privacy provisions, according to HIPAA, have been adequately reviewed, discussed, and documented in the IRB meeting minutes. The provisions include determination of waiver of authorization, as well as review of the subject authorization, as appropriate;
- Evaluation of continuing review discussions to assure that they are substantive and meaningful, and that no lapse in approval has occurred since the prior IRB review;
- Review of the IRB electronic files to assure retention of appropriate documentation and consistent organization of the IRB files according to current policies and procedures;
- Review of the IRB electronic files to assure all fields are completed accurately;
- Review of the time intervals between various steps of the IRB submission-to-approval process;
- Assessment of the number of reviews required for IRB approval;
- Assessment of the reasons requiring multiple reviews for IRB approval; and
- Other monitoring or auditing activities deemed appropriate.

The goal of these reviews is to identify and correct any areas of deficiency in order to provide a service to the research investigators while also ensuring the protection of the human research subjects. The results may impact current practices and may require additional educational activities, both for the staff and the research community.

PERFORMANCE METRICS

Metrics are gathered by units involved in NYU Langone Health's HRP to measure performance and may be used to improve the HRP.

IRB Metrics
The average number of days from receipt of Principal Investigators' applications to the date of IRB approval is measured as well as the time from receipt of submission to the first IRB review and the amount of time a submission is with the IRB or the Principal Investigator. These measurements of quality, efficiency and effectiveness are available and reported to the IO and IRB Chairs.

QIA Division Metrics
The results of QIA Division activities are compiled by the IRB Operations team and reported to the IRB and the IO, as well as to other units within NYU Langone as appropriate. These results provide a quantitative and qualitative measurement and insight of both the effectiveness of the QIA Division activities within the HRP in addition to expected outcome of enhanced investigator compliance.

Education Metrics
Clinical Research Foundational Program:
NYU Langone Health measures through the Clinical Research Foundational Program:

(1) Learner understanding of the content through polling results and results of a test taken by each learner at the conclusion of the program. The test results are used to evaluate problematic content within courses and helps to improve the content/explanation as needed in future courses. Test results also indicate the number of learners who were successful in completing the program.

(2) Learner survey (post course): This survey helps assess overall learner satisfaction with the material, and quality of the course presentation. It also allows the learner to provide feedback for additional comments and improvement of the course.

(3) Supervisor survey (1 month post course): This survey is sent to learner's supervisors and inquires whether they have observed the learner as having an improved understanding of the research process. This metric helps evaluate the impact of the course and its relevance on the learner's daily work performance.

Principal Investigator Development and Resources (PINDAR): Principal Investigators are asked to (voluntarily) complete a survey at the end of the program and are invited to complete a second survey after approximately three months. Both surveys allow for self-assessment of the course, their perceptions of the relevance of the material covered in PINDAR, and their perception of the quality of the teaching while providing an opportunity for direct feedback most relevant to each PI.

Clinical Research Support Unit (CRSU) Metrics
The CRSU is responsible for the administration of industry-funded clinical research/trials, from pre-award feasibility to post-award financial management, as well as clinical research billing compliance. As such, the CRSU tracks metrics on start-up/activation cycle time for new trials as well as revenue generation and cost recovery related to ongoing activity. Billing compliance metrics track volume of misrouted hospital charges to ensure coverage analysis is performed according to Medicare regulations and research subjects are not held responsible for research billable costs.

5. INSTITUTIONAL REVIEW BOARDS

The NYU Langone Health IRBs are administrative bodies established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of NYU Langone Health. There are currently seven (7) Institutional Review Boards: five at NYUGSoM and two at NYUGLISoM. Each IRB functions identically, has equivalent expertise, and reviews all Human Subjects Research conducted at NYU Langone Health or other organizations conducting studies under its jurisdiction. The IO, the Senior Director of HRP, and the respective IRB Chairs review the activity of the IRB on at least an annual basis and make a determination as to the appropriate number of review boards and meetings that are needed for the institution.

The two principal responsibilities of the IRB are (1) protecting research subjects from undue risk and (2) protecting research subjects from deprivation of personal rights and dignity. These protections are best assured by consideration of three principles as set forth in the Belmont Report, which are referred to as Respect for Persons, Beneficence, and Justice, and are the touchstones of ethical research:

The primary purpose of the IRB is to review research protocols involving human subjects and to assure protection of the safety, welfare and right of the subjects.

The mission of the IRB is to:

- safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are protected;
- determine and certify that all projects reviewed by the IRB conform to the policies and procedures set forth in this document, including all applicable regulations regarding the health, welfare, safety, rights, and privileges of human subjects;
- provide timely and high quality education, review and monitoring of human research projects; and
- facilitate excellence in Human Subjects Research.

The NYU Langone Health IRB Operations Office (as described below) includes mechanisms to:

- establish a formal process to monitor, evaluate and continually improve the protection of human research subjects;
- dedicate resources sufficient to do so;
- exercise oversight of research protection;
- educate investigators and research staff about their ethical responsibility to protect research subjects;
- assist the investigators in complying with federal and state regulations; and
- when appropriate, intervene in research and respond directly to concerns of research subjects.

5.1 AUTHORITY OF THE IRB

The NYU Langone Health IRBs review and have the authority to approve, require modifications in, or disapprove all research activities conducted under the auspices of NYU Langone Health and under their jurisdiction, e.g., Exempt research including those activities for which limited IRB review is a condition of exemption. The IRB also has the authority to suspend, place restrictions on, or terminate approvals of research activities that fall within its jurisdiction that are not being conducted in accordance with IRB requirements, or that have been associated with unexpected serious harm to subjects.

The IRB ensures that appropriate safeguards exist to protect the rights and welfare of research subjects [45 CFR 46.111]. In fulfilling these responsibilities, the IRB reviews all research documents and activities that bear directly on the rights and welfare of the subjects of proposed research.

Examples of IRB review documentation include, *inter alia:* protocols, consent/assent document(s) and, for studies conducted under the Investigational New Drug ("IND") regulations, the investigator's brochure(s), tests, surveys, questionnaires and similar measures, and recruiting documents.

Before any human subject becomes involved in research at NYU Langone Health, the IRB will properly consider:

i. risks to the subject and others
ii. anticipated benefits to the subject and others
iii. importance of the knowledge that may reasonably be expected to result from the study
iv. informed consent process to be employed

The IRB has the authority to suspend, place restrictions upon, or terminate approval of research activities that fall within its jurisdiction that:

v. are not being conducted in accordance with IRB requirements, or
vi. that have been associated with serious harm to subjects

The IRB has the authority to observe (or delegate a third party to observe) the consent process and the research if the IRB deems this necessary.

5.2 JURISDICTION OF THE IRB

The jurisdiction of NYU Langone Health IRBs, and any other IRB to which NYU Langone Health cedes IRB review, extends to all research (funded and unfunded) involving human subjects conducted at NYU Langone Health, as well as research conducted elsewhere by NYU Langone Health faculty, staff, and students, including research where involvement of human subjects falls within one or more exempt categories (see Categories of Research Permissible for Exemption). Each IRB may act as the reviewing IRB for human subjects research conducted by any part of NYU Langone Health, including research conducted by NYU LISoM faculty at NYUGLISoM and research conducted by NYUGSoM faculty at NYUGSoM.

5.3 IRB RELATIONSHIP WITH OTHER HRP UNITS

The NYU Langone Health IRBs function independently of, but in coordination with, other institutional regulatory committees. The IRB, however, makes independent determinations regarding approval or disapproval of a protocol based upon whether or not human subjects are adequately protected. The IRB retains review jurisdiction over all research involving human subjects that is conducted, supported, or otherwise subject to regulation by any federal department or agency that adopted the human subjects regulations.

Research previously reviewed and approved by the IRB may be subject to review and disapproval by officials of the institution. However, officials of the institution have no authority to approve research previously disapproved by the IRB.

5.4 NYU LANGONE HEALTH IRB RELATIONSHIPS WITH OTHER INSTITUTIONS

DEFINITIONS

"COOPERATIVE RESEARCH"

means research projects covered by HHS Common Rule regulations and that involve more than one institution. Each institution conducting a Cooperative Research project is responsible for safeguarding the rights and welfare of its subjects. The sites may be conducting identical activities or implementing different aspects of the same protocol, and the research may be taking place within the U.S. or internationally.

"EXTERNAL IRB"

for purposes of this Policy, means an IRB outside of the institution that oversees a research study or studies for the institution. An External IRB can be an independent (commercial) IRB or an IRB of another institution (that may or may not serve as an sIRB). When an institution uses an IRB outside their institution to review their research studies, this is called "ceding" or "deferring" IRB review to an External IRB.

"EXTERNAL RELATIONS"

is the division within the HRP which oversees services associated with use of External IRBs or use of NYU Langone Health's IRB as the IRB of record. External Relations is comprised of Reliance and IRB professionals who provide either clearance for unaffiliated institutions to use NYU Langone Health's IRB as Single IRB or for NYU Langone Health to cede review authority to an External IRB.

"MULTI-SITE PROJECT"

for purposes of the Single IRB Policy, means a sub-set of non-exempt Cooperative Research where the same research procedures (i.e., operating under the same protocol) are conducted at two (2) or more U.S. research sites under the control of a participating investigator at each site. A Multi-Site Project typically involves a lead site (lead PI) that manages the administrative functions of the project (typically, through subawards or contracts to participating sites) in addition to conducting the same research procedures as the participating sites. The sites may be conducting identical activities or implementing different aspects of the same protocol. A Multi-Site Project could be a clinical trial, an observational study, or a basic clinical research study.

"SINGLE IRB" OR "sIRB"

means the IRB of record for non-exempt Cooperative Research (defined above), selected on a study-by-study basis.

POLICY PURPOSE

The purpose of this Policy is to establish when an sIRB must be used and under what circumstances NYU Langone Health's IRB will serve as sIRB for a study. The Policy also provides guidance for Principal Investigators who wish to utilize a non-NYU Langone Health (external) IRB for ethical oversight for a study.

SINGLE IRB/SIRB POLICY

Use of sIRBs – When an sIRB is required

Consistent with the 2020 Common Rule (45 CFR §46.114, Cooperative Research) and NIH guidelines, an sIRB

is required for review of Cooperative Research and Multi-Site Projects that received initial IRB approval on or after January 20, 2020, that meets the following criteria:

- The research study is funded by any federal agency;
- The proposed work meets the definition of both "research" and involves "human subjects" as defined by DHHS regulations (45 CFR § 46.102); and
- The proposed work involves multiple (at least 2 or more) **domestic** sites engaged in human subjects activities.

The research could be a clinical trial, an observational study, or a basic clinical research study.

Any exceptions to the requirement for use of an sIRB for Cooperative Research or a Multi-Site Project must be obtained in writing from the Federal Agency funding the research and provided to External Relations.

When NYU Langone Health Will Serve as sIRB

Requests for NYU Langone Health to act as an sIRB must be submitted to External Relations, which will determine if the request meets the criteria outlined below. If approved, External Relations will oversee the onboarding of all relying sites, including ensuring that appropriate reliance (or authorization) agreements are in place, set-up of the sites in relevant systems, and IRB review and approval of the relying sites.

Criteria for NYU Langone Health Serving as Single IRB

1. Notification of Proposal. NYU Langone Health Principal Investigators submitting any federal grant applications may propose the NYU Langone Health IRB as the sIRB for a study but must first obtain approval from External Relations prior to grant submission. Notification must be made through a form available on NYU Langone Health's intranet page ("Selecting the NYU Langone Health IRB as the sIRB of Your Study"). Single IRB service fees must be assessed and budgeted for in the relevant grant application.

2. When NYU Langone Health is the prime recipient of the grant award (awardee), NYU Langone Health's IRB will act as sIRB.

3. On a case-by-case basis, the Senior Director of HRP or designee will consider requests to rely on an External IRB as the sIRB of a proposed study to be conducted at NYU Langone Health.

Foreign and Other Sites

NYU Langone Health will not serve as sIRB to foreign sites, Veteran's Administration ("VA") sites, sites involving tribal nations, and sites for which review by NYU Langone Health's IRB as sIRB is prohibited by federal, tribal, or state regulations, or other policies. The specific law, regulation, or policy should be cited in the applicable grant application or contract proposal's sIRB plan if NYU Langone Health cannot serve as the sIRB. A study may involve sites that must comply with the NIH sIRB policy as well as other sites that are not required to comply.

Roles and Responsibilities

1. Lead Principal Investigator

   In addition to the Roles and Responsibilities described in Section 16, for studies where NYU Langone Health's IRB is serving as the sIRB, the lead Principal Investigator for a study that is utilizing the sIRB is responsible for oversight of onboarding, reliance agreements, and IRB review

and approval of all relying sites. The Principal Investigator must maintain and share all relevant study materials with each relying site and ensure that all relying institution Site investigators are trained on the protocol and have access to NYU Langone Health HRP Policies and Procedures and the systems through which relying sites submit to the NYU Langone Health IRB for review. Principal Investigators must initiate the SMART IRB Reliance Agreement request. Once reliance is in place, the Principal Investigator must ensure that all relying site submissions are submitted to the IRB in Research Navigator. The Principal Investigator must collect enrollment data and ensure timely reporting of all Continuing Review information, and ensure the relying sites report all reportable events consistent with these Policies and Procedures.

2. Site Principal Investigator

   Site Principal Investigators ("Site PI's") must follow all local and state requirements at their local institutions when relying on NYU Langone Health's IRB as sIRB. The Site PI must communicate any applicable local or state requirements to the NYU Langone Health sIRB. The Site PI is responsible for creating and maintaining accounts as required by the NYU Langone Health sIRB in all tracking and IRB submission systems, and to follow NYU Langone Health Policies and Procedures for all submissions and reportable events.

3. Relying Institution

   Any institution for whom the NYU Langone Health IRB acts as the sIRB must comply with the applicable provisions of NYU Langone Health's IRB Policies. When the NYU Langone Health IRB acts as an sIRB, the particular characteristics of the unaffiliated institution's local research context will be considered. It is the relying site's responsibility to provide the NYU Langone Health IRB with such information. The relying institution is required to maintain an active Federalwide Assurance (FWA) and communicate any changes to the local research context or site information to the reviewing sIRB.

   Relying sites are responsible for maintaining an active list of study team members working on the research in accordance with local requirements and policies. They are also responsible for ensuring relevant Conflicts of Interest have been managed, expertise of the study team is sufficient to conduct the proposed research, and education requirements are met. Relying sites must ensure that any other applicable local policies and ancillary reviews are complied with prior to the research beginning at the relying institution. Any relevant concerns, determinations, or decisions must be communicated to the sIRB.

sIRB Review Process

The sIRB review process will include reviews as follows:

1. **Initial review.** The study will be reviewed by the NYU Langone Health IRB in accordance with all NYU Langone Health IRB requirements and policies. This initial review will include approval of the main site for IRB purposes (NYU Langone Health) and may include review and approval of relying sites, if the sites have completed the necessary requirements including a signed reliance agreement. IRB approval for NYU Langone Health as the main site does not serve as IRB approval for any relying sites. The approval letter will reference any relying sites that have been approved in the initial review.

2. **Relying site review.** Relying sites that were not approved in the initial review will be on-boarded on a site-by-site basis and receive their own IRB approval letter and any relevant sIRB-approved materials. Any modifications affecting local site materials must be submitted by the relying site principal investigator for IRB review and approval.

3. **Continuing review.** Continuing Review approval of sIRB studies is granted for the NYU Langone Health site and all active relying sites at the time of renewal. Relying sites must submit individually to the NYU Langone Health IRB to obtain site-specific Continuing Review approval letters and stamped materials.

4. **Reportable new information.** All relying sites have an obligation to report new information consistent with Section 8.8 of this Policy. Should the IRB determine the event requires further reporting to federal agencies, relying institutions will be notified of this decision and given the opportunity to review the federal correspondence consistent with the terms in the applicable reliance agreement.

5. **Notification of certain IRB decisions.** In the event that the NYU Langone Health IRB makes a finding of serious noncompliance, continuing noncompliance, or unanticipated problems that occurred in the course of the conduct of the study at a participating site, the NYU Langone Health IRB will convey this information to the Site PI and to OHRP or other federal agencies as appropriate. These notifications will be made in writing, with copies to the participating site's IO and IRB director or reliance coordinator as specified in the reliance agreement, and NYU Langone Health's IO, PI, Sponsored Programs Administration Director, and Human Research Protections Senior Director.

Local Context of Relying Sites

When NYU Langone Health's IRB reviews research on behalf of another institution, the characteristics of the unaffiliated institution's local research context must be considered, using the institution's local research context, and if necessary, subsequent review by appropriate designated institutional officials, such as the IO, HRP Senior Director, Chairperson and/or other IRB members.

POLICY ON NYU LANGONE HEALTH'S USE OF AN EXTERNAL IRB

NYU Langone Health may choose, on a case-by-case basis, to cede or share its IRB oversight responsibilities of certain research conducted at or under the auspices of NYU Langone Health to an External IRB. This Policy describes when an External IRB may be used.

External Relations reviews requests to cede review of a study to an External IRB and determines if the request meets the criteria outlined below. If the request is approved, External Relations will negotiate reliance agreements and provide institutional clearance for all studies for which approval is granted to cede review to an External IRB.

Process – Requesting Use of an External IRB and Criteria for Approval

1. Researchers and research teams are not authorized to cede IRB review. The decision to cede oversight responsibilities must be made by the HRP Senior Director or their designee in consultation with the IO, as needed. **Any Principal Investigator who wishes to make use of an External IRB for review of a study must first contact the HRP Office for approval and initiation of a written agreement.**

2. Use of an External IRB for review of NYU Langone Health research is generally permitted if:

    - The research is industry-initiated and requires the use of a central IRB; or
    - The research is a federally funded multicenter trial that requires the use of another institution's IRB consistent with federal regulations described in 45 CFR §46.114.

Other than as permitted above, any exceptions to allowing use of an External IRB may be considered on a case-by-case basis.

3. In addition to the criteria above, when determining which External IRB NYU Langone Health may cede to, the following will be considered:

    - Qualifications and expertise of the proposed External IRB;
    - Whether the External IRB is accredited by the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRP) or equivalent; and
    - Any other relevant information about the IRB under consideration, such as previous audits and findings of non-compliance.

4. NYU Langone Health will not cede or share its IRB oversight responsibilities to an External IRB that is not AAHRPP-accredited or cannot demonstrate through written policies and procedures that its standards are substantially equivalent to ensure the research will be reviewed appropriately.
5. When NYU Langone Health relies on an External IRB, the External IRB's policies and procedures may be reviewed by External Relations to ensure that they meet NYU Langone Health IRB standards. If the External IRB is accredited by AAHRPP, then it will be assumed that the NYU Langone Health standards are being met, provided that all local context and institutional requirements are considered and followed, as appropriate.
6. Reliance agreements. A formal relationship between NYU Langone Health and the External IRB must be established through a reliance agreement.

    NYU Langone Health is a member of the SMART IRB Master Reliance Agreement. For all research where NYU Langone Health's IRB acts as the sIRB or where NYU Langone Health cedes to an External IRB, the SMART IRB agreement should be used. Requests to use another individual IRB reliance agreement will be considered on a case-by-case basis.

    NYU Langone Health also has individual master reliance agreements with several commercial IRBs, to be used for research meeting criteria to use an External IRB as described above. Final decisions on reliance agreements are made by the IO or HRP Senior Director.

5.5 NYU LANGONE HEALTH AS COORDINATING CENTER

When NYU Langone Health serves as the coordinating center for a multi-center protocol, the study chair or equivalent at NYU Langone Health shall submit the protocol and other study documents to the NYU Langone Health IRB for review and approval, unless such protocol relies on an External IRB in accordance with a written agreement. The NYU Langone Health IRB will require that study chair or equivalent ensure that each relying site receives approval from an IRB with jurisdiction over that site prior to initiation of the research at that site. At the time of initial review, the IRB will assess the procedures for dissemination of protocol information to all relying sites. Assessment of protocol information includes, *inter alia,* unanticipated problems involving risks to subjects, protocol modifications, and interim findings.

In the conduct of Cooperative Research projects, NYU Langone Health acknowledges that each institution is responsible for safeguarding the rights and welfare of its human subjects, and further for ensuring compliance with the applicable federal regulations. When a cooperative agreement exists, NYU Langone Health may enter into a joint review arrangement, rely on the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

When an investigator plans to conduct research at sites external to NYU Langone Health and the external site's IRB plans to defer review to NYU Langone Health's IRB, arrangements must be made for NYU Langone Health's IRB to be the IRB of record for the project and arrangements must be made for communication between the IRB and the external site.

5.6 IRB OPERATIONS

In addition to the leadership structure described above, other IRB Operations staff members are listed below. IRB Operations staff for NYU Langone Health will comply with all ethical standards and practices.

IRB OPERATIONS ("IRB OPS")

IRB Operations is the office that manages the NYU Langone Health IRBs. All NYU Langone Health IRB Operations staff are selected by the Senior Director of HRP and/or Director, IRB Operations who has day-to-day oversight over IRB and the IRB Operations office. The Director of IRB Operations reports to the Senior Director, HRP.

Additionally, IRB Operations is staffed by Senior Scientific Managers, Scientific Managers, IRB Review Specialists, Analysts, Coordinators, and Education and Training Specialists. The qualification criteria, duties and responsibilities for all staff are found in their respective job descriptions. IRB Operations staff performance is evaluated on an annual basis.

The general criteria for selection of the IRB Operations staff includes: (1) background knowledge in clinical research for professional staff, (2) high-level organizational, analytical and administrative abilities, and (3) customer service-oriented skills.

6. IRB MEMBERSHIP

The Senior Director, HRP, in coordination with the IRB Chair and the IO, will identify potential candidates in consideration of IRB membership. NYUGSoM and NYU LISoM Department Chairs and/or Division Chiefs may also be requested to identify potential candidates for appointment to the IRB Board.

On an ongoing basis, the Senior Director, HRP will monitor the membership and composition of the IRB and make recommendations on the appointment of members to the IO in order to meet regulatory and organizational requirements.

Appointments of IRB Board members are made by the Senior Director, HRP or designee, for a term of one year with automatic renewal.

Requirements for IRB membership and composition will be in compliance with DHHS regulations (45 CFR 46.107) and FDA regulations (21 CFR 56.107). IRB members are selected based on appropriate diversity, including consideration of race, gender, cultural backgrounds, specific community concerns in addition to representation by multiple, diverse professions, knowledge and experience with vulnerable subjects, and inclusion of both scientific and non-scientific members. The structure and composition of the IRB must be appropriate to the amount and nature of the research that is reviewed. Every effort is made to have member representation that has an understanding of the areas of specialty that encompasses most of the research performed at the IRB. The IRB has procedures (see Section 5. Institutional Review Boards) that specifically outline the requirements of protocol review by individuals with appropriate scientific or scholarly expertise.

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

The IRB must promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects; and possess the professional competence necessary to review specific research activities. A member of the IRB may fill multiple membership position requirements for the IRB.

6.1 COMPOSITION OF THE IRB

The IRB will at all times consist of at least five members with its guiding principle to promote complete review of research activities commonly conducted by the institution and any other organization under its jurisdiction.

The IRB will be sufficiently qualified through the experience and expertise of its members (professional competence), and the diversity of its members, including race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.

The IRB will be able to ascertain the acceptability of proposed research in terms of institutional commitments (including applicable institutional policies and resources) and federal regulations, applicable law, and standards of professional conduct and practice. The IRB will therefore include persons knowledgeable in these areas.

Since the IRB regularly reviews research that involves a category of subjects that is vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, consideration is given to the inclusion of one or more individuals on the IRB who are knowledgeable about, and experienced in, working with these categories of subjects. When protocols involve vulnerable populations, the review process will include one or more individuals who are knowledgeable about or experienced in working with these subjects, either as IRB members or as consultants (see: Use of Consultants (Outside Reviewers)). Prior to the meeting, IRB Operations staff will review the agenda to ensure that the membership present for the meeting has the appropriate expertise and experience with any vulnerable populations that are included in the protocols being reviewed.

Every nondiscriminatory effort will be made to ensure that the IRB does not consist entirely of men or entirely of women, including the institution's consideration of qualified persons of both gender, so long as no selection is made to the IRB on the basis of gender. The IRB shall not consist entirely of members of one profession. The IRB includes at least one member whose principal concerns are in scientific areas and at least one member whose principal concerns are in nonscientific areas.

The IRB includes at least one member who is not otherwise affiliated with the institution and represents a member of the community NYU Langone Health serves (non-affiliate member). The member cannot be a part of the immediate family of a person affiliated with the institution.

The IRB may not have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

The IRB, in its discretion, may invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that which is available on the IRB. These individuals may not vote with the IRB.

One member may satisfy more than one membership category.

The Senior Director, HRP, Associate Director and Scientific Managers of the NYU Langone Health's IRB Operations may be voting members of the IRB.

IRB members are appointed for renewable one to three year terms. On an ongoing basis, the Senior Director, HRP will monitor the membership and composition of the IRB and make recommendations on the appointment of members to the IO in order to meet regulatory and organizational requirements.

Staff from the NYU Langone Health's Sponsored Programs Administration, Office of Development and Alumni Affairs, or Technology Opportunities & Ventures are prohibited from serving as members of the IRB or carrying out day-to-day operations of the review process. Individuals from these offices may, however, provide information to the IRB and attend IRB meetings as guests.

6.2 APPOINTMENT OF MEMBERS TO THE IRB

The IRB Chairs, Vice Chairs and/or the Senior Director, HRP identify a need for a new or replacement member, or alternate member. The IRB membership may nominate candidates and forward the names of the nominees to the IO. Department Chairs and others may forward nominations to the IO, the IRB Operations, or the respective IRB Chairs or Vice-Chairs.

For faculty membership appointments, the Senior Director, HRP will contact the nominee. If there are no nominees, the appropriate NYUGSoM or NYU LISoM Department Chairs or Program Directors will be contacted in writing by the IO or the Senior Director, HRP concerning the vacancies and solicit nominees from the Department Chairs or Program Director.

The final decision in selecting a new member is made by the Senior Director, HRP, who may consult with the IO and the applicable IRB Chairs.

Appointments are made for renewable one to three-year periods of service. Any change in appointment, including reappointment or removal, requires notification. Members may resign by written notification to the appropriate IRB Chair and/ or the Senior Director, HRP.

On a periodic basis, the IRB Chairs and the Senior Director, HRP will review the membership and composition of the IRB to determine whether or not the IRB continues to meet regulatory and institutional requirements. Required changes in IRB membership will be reported to the OHRP.

6.3 ALTERNATE MEMBERS

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

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

6.4 USE OF CONSULTANTS (OUTSIDE REVIEWERS)

When necessary, the IRB Chairs or the Senior Director, HRP may solicit individuals from the NYU Langone Health or the general community who are competent in specialized areas to assist in the review of issues or

protocols requiring scientific or scholarly expertise beyond, or in addition to, that available on the IRB. The need for an outside reviewer is determined in advance of the IRB meeting by the Senior Director, HRP or the IRB Chair or may be recommended by the primary reviewer. IRB Operations will ensure that all relevant materials are provided to the outside reviewer prior to the convened meeting.

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

Written statements of outside reviewers will be kept in IRB records and filed with the relevant protocol. Key information provided by outside reviewers at convened meetings will be documented in the meeting minutes.

The Senior Director, HRP reviews the conflict of interest policy for IRB members with consultant(s) (see: IRB Member Conflicts of Interest). The consultant(s) must verbally confirm to the Senior Director, HRP that no conflicts of interest exist prior to review. Individuals who have a conflicting interest or whose spouse or family members have a conflicting interest with the sponsor of the research will not be invited to provide consultation.

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

6.5 DUTIES OF IRB MEMBERS

The agenda, submission materials, protocols, proposed informed consent forms and other appropriate documents are distributed to IRB members at least one week prior to the convened meetings at which the research is scheduled to be discussed in order to ensure full participation in the review of each proposed project. IRB members are expected to treat the research proposals, protocols, and supporting data confidentially. All copies of the protocols and supporting data are returned to the IRB Operations staff at the conclusion of the review for professional document destruction.

6.6 ATTENDANCE REQUIREMENTS

IRB Members must attend a minimum of ten meetings annually, and should attend all meetings for which they are scheduled. If a member is unable to attend a scheduled meeting, that member should inform the IRB Chair, Vice Chair, or an IRB Operations staff member. If the inability to attend will be prolonged, a request for an alternate to be assigned may be submitted to the Chair or the Senior Director, HRP. If an IRB member is to be absent for an extended period of time, such as for a sabbatical, he or she must notify the IRB at least thirty (30) days in advance so that an appropriate replacement can be obtained. The replacement can be temporary, for the period of absence, or permanent if the member is not returning to the IRB. If the member has a designated alternate (see: Alternate Members), the alternate can serve during the principal member's absence, provided that the IRB receives advance notice.

6.7 TRAINING/ONGOING EDUCATION OF NYU LANGONE HEALTH'S IRB CHAIRS AND IRB MEMBERS IN REGULATIONS AND PROCEDURES

A vital component of a comprehensive human research protection program is an education program for the IRB Chairs and the IRB members. NYU Langone Health is committed to providing training and an on-going

educational process for NYU Langone Health's IRB members and the staff of the NYU Langone Health's IRB Operations, related to ethical concerns and regulatory and institutional requirements for the protection of human subjects (see *Education and Training Plan*).

ORIENTATION

New IRB members, including alternate members, will meet with an IRB Chair and the respective Senior Director, HRP for an informal orientation session. New members are given an IRB Handbook that includes:

- The Belmont Report
- NYU Langone Health Human Subjects Protections Policies and Procedures
- Federal regulations relevant to the IRB

New members are required to complete the Initial Education requirement (discussed in the next section) prior to serving as primary reviewer.

INITIAL EDUCATION

All new IRB members will complete the web-based NYU Langone Health Human Subjects Training Module.

CONTINUING EDUCATION

To ensure that oversight of human research is ethically grounded and that the decisions made by the IRB are consistent with current regulatory and policy requirements, training is continuous for IRB members throughout their service on the IRB. Educational activities include, but are not limited to:

- in-service training at monthly IRB meetings and on an annual basis for topics of significance
- review of appropriate publications
- identification and dissemination of new information that might affect the human research protections, including emerging laws, regulations, policies, procedures, and ethical and scientific issues to IRB members via email, mail, or during IRB meetings
- unlimited access to the IRB Operations resource library
- completion of web-based NYU Langone Health Human Subjects Training Module once every three (3) years

Annual review of IRB members' performance will include confirmation of their compliance with these education requirements. Members who have not fulfilled their education requirements will receive up to three (3) reminders to complete their training within thirty (30) days of notification. In the event of continued non-compliance, the IRB member may be removed at the discretion of the Senior Director, HRP and IRB Chair.

IRB OPERATIONS STAFF TRAINING

All new IRB Operations staff will meet with the Director, IRB Operations for a formal introduction to the IRB and staff members' responsibilities. At this session, the new staff will be given an IRB Handbook that includes:

- The Belmont Report
- NYU Langone Health Human Subjects Protections Policies and Procedures
- Federal regulations relevant to the IRB

The IRB Operations staff is required to complete the entire CITI Course in the Protection of Human Research Subjects once every three (3) years and the NYU Langone Health Human Subjects Training module. Staff will be expected to attend PRIM&R or OHRP training at least annually.

The IRB Operations staff will be expected but not required to become CIP-certified within a two-year period of employment. In lieu of CIP-certification, staff may demonstrate proficiency and equivalent knowledge through their day-to-day performance as assessed by the IRB Associate Director.

Failure of IRB Operations staff to fulfill their training and education requirements will become part of their employee evaluation. Continued non-compliance may lead to implementation of a corrective action plan, termination, or other disciplinary action.

6.8 LIABILITY COVERAGE FOR IRB MEMBERS

The NYU Langone Health's insurance coverage applies to NYU Langone Health employees, any person authorized to act on behalf of the NYUGSoM IRB or the NYUGLISoM IRBs, and any person who acts within the scope of their employment or authorized activity on behalf of NYU Langone Health.

6.9 REVIEW OF IRB MEMBER PERFORMANCE

IRB members' performance will be reviewed on an annual basis by the respective IRB Chairs and Senior Director, HRP. Formal feedback based upon this evaluation will be provided to IRB members in writing with an opportunity to discuss in person. Members who are not acting in accordance with the IRB mission or policies and procedures, or IRB members who have an undue number of absences, will be removed.

6.10 IRB MEMBER CONFLICTS OF INTEREST

IRB members and consultants will not participate in any IRB action, including the initial and continuing review of any project, in which the member has a conflicting financial or other interest, except to provide information requested by the IRB. IRB members are required to self-identify conflicts of interests. A primary reviewer or expedited reviewer with a conflict of interest must notify the IRB Operations staff, and the IRB Operations staff will, in turn, re-assign the protocol to another IRB member.

An IRB member is considered to have a conflicting interest when the IRB member or an immediate family member (defined as having a relationship to a person, whether by blood, law, or marriage, as a spouse, parent, child, grandparent, grandchild, stepchild, or sibling) of the IRB member:

- has an involvement in (or is directly supervising) a research project being reviewed by the IRB;
- is the project director, or a member of the research team;
- has a financial interest (for example, a financial interest in the sponsor or the product or service being tested) in the research whose value cannot be readily determined or whose value may be affected by the outcome of the research;
- has a financial interest in the research with value that exceeds $10,000 or 5% ownership of any single entity when aggregated for the IRB member and their immediate family;
- has received or will receive any compensation whose value may be affected by the outcome of the study;
- has a proprietary interest in the research (property or other financial interest in the research including, but not limited to, a patent, trademark, copyright or licensing agreement);
- has received payments from the sponsor that exceed $10,000 in one year when aggregated for the IRB member and their immediate family;
- is an executive or director of the agency or company sponsoring the research; and/or
- any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a protocol.

IRB members who have a conflicting interest in a research study will be excused from the meeting room when the IRB reviews the research, except when otherwise requested to provide information to the IRB. The IRB Chair will allow for Board discussion to commence upon the conflicted member's removal from the meeting. The conflicted member is not counted toward the quorum and his/her absence during the discussion and vote on the protocol will be noted in the IRB meeting minutes, with an indication that a conflict of interest was the reason for the absence.

If the conflict of interest status of an IRB member changes during the course of a study, the IRB member is required to declare such conflict to the IRB Chair and/or Senior Director, HRP. Additional information can be found in NYU Langone Health's *Policy on Conflict of Interest in Business Affairs*.

6.11 REPORTING AND INVESTIGATION OF ALLEGATIONS OF UNDUE INFLUENCE

If an IRB Chair, IRB member, or IRB Operations staff member feels that the IRB has been unduly influenced by any party, they shall make a confidential report to the IO, who can determine corrective action, depending on the circumstances.

The official receiving the report or his/her designee will conduct a thorough investigation and corrective action will be taken to prevent additional occurrences.

7. IRB RECORDS

The IRB will prepare and maintain adequate documentation, in printed form or electronically, of the IRB's activities.

IRB records will include continuing review activities, including the rationale for conducting continuing review of research that otherwise would not require continuing review as described in 45 CFR 46.108(f)(1), and copies of all correspondence between the IRB and investigators. Statements of significant new findings provided to subjects must be maintained with the related research proposal and, when reviewed at an IRB meeting, such statements must be documented in the minutes.

Documentation of verified exemptions consists of the reviewer's written concurrence that the activity described in the investigator's request satisfies the conditions of the cited exemption category.

IRB records for initial and continuing review by the expedited procedure must include: the specific permissible category; a description of action taken by the reviewer, and any determinations required by the regulations and protocol-specific findings supporting those determinations. IRB records must also document the rationale for an expedited review's determination under 45 CFR 46.110(b)(1)(i) that research appearing on the expedited review list described in 45 CFR 46.110(a) is more than Minimal Risk.

IRB records must document any determinations required by the federal regulations and protocol-specific findings supporting those determinations.

All records must be accessible for inspection and copying by authorized representatives of the FDA, OHRP, sponsors, and other authorized entities at reasonable times and in a reasonable manner.

IRB records must also include documentation of the responsibilities that NYU Langone Health and the IRB will undertake to ensure compliance with the requirements of 45 CFR 46.

7.1 IRB RECORDS

Records that will be maintained by the IRB include, but are not limited to:

- Written IRB operating procedures
- IRB membership rosters
- IRB training records. For NYU Langone Health's IRBs, the IRB Education Coordinator maintains accurate records listing research investigators, IRB members, and IRB Operations staff that have fulfilled the institution's human subject training requirements. Electronic copies of documentation are maintained in the official IRB records maintained by IRB Operations.
- IRB correspondence (other than protocol related)
- IRB Study Files for each study. Documents included in Study Files are listed in Section 7.2 (IRB Study Files) below.
- Documentation of Emergency Exemption from Prospective IRB Approval. (21 CFR 56.104(c))
- Documentation of Exceptions from Informed Consent Requirements for Emergency Use of a Test Article ((21 CFR 50.23)
- Documentation of verified exemptions (including documentation of initial and continuing review)
- Documentation of convened IRB meetings minutes
- Documentation of review by an external/another institution's IRB when appropriate
- Documentation of cooperative review agreements, e.g. Memoranda of Understanding (MOUs)
- Federal Wide Assurances (FWAs), Protocol violations submitted to the IRB, Quality assurance reviews

Documentation that must be maintained for studies reviewed by external IRBs includes:

- On-line access to all applicable protocol documents
- MOU/agreements of IRB services
- Workflow/SOPs
- Notes/documents pertaining to administrative reviews

7.2 IRB STUDY FILES

The NYU Langone Health IRBs maintain Study Files in an electronic system ("Research Navigator") that holds complete records for each human research study that was active as of November 2013 or later. Previous records are kept in an electronic documents archive for at least three years, or in a combination of the archive system and the current electronic system. Research Navigator issues each study a unique study number which is used throughout the institution to refer to the study throughout its entire operational life. Research Navigator maintains all submission forms, study-related documents and all official communications to and from the IRB to study staff. Additionally, each study team shall keep copies of these files in the Principal Investigator's project file.

Study Files include (but are not limited to):

- Protocol and all other documents submitted as part of a new protocol application;
- Protocol and all other documents submitted as part of a request for continuing review/termination of research application. This also includes progress reports, statements of significant new findings provided to subjects, reports of injuries to subjects;
- Documents submitted and reviewed after the study has been approved, including reports of modifications to research/amendments and adverse event reports;
- Copy of IRB-approved consent form;
- DHHS-approved sample consent form document and protocol, when they exist;
- IRB reviewer forms (when expedited review procedures are used) and scientific reviewer forms (where applicable);

- Documentation of type of IRB review;
- For expedited review, documentation of any determinations required by the regulations and protocol- specific findings supporting those determinations, including:
    - waiver or alteration of the consent process
    - research involving pregnant women, fetuses, and neonates
    - research involving prisoners
    - research involving children
    - research involving persons with impaired cognitive function;
- Documentation of all IRB review actions;
- Notification of expiration of IRB approval to the Principal Investigator and instructions for submitting relevant continuing review materials;
- Notification of suspension of research;
- Correspondence pertaining to appeals;
- Copies of approval letters and forms that describe what Principal Investigator must have before beginning the study;
- IRB correspondence to and from study investigators;
- All other IRB correspondence related to the research;
- For studies of medical devices, a report of prior investigations;
- Reports of Unanticipated Problems involving risk to subjects or others and adverse events; and
- A log of each submission's administrative history and communications within Research Navigator that take place between the IRB and the study team.

7.3 MINUTES OF AN IRB MEETING

Documentation of proceedings at a convened IRB meeting must be written and available for review by the next regularly scheduled IRB meeting date. After ratification of the minutes by the Board members, if it is determined that revisions/corrections are necessary, the minutes will be amended and presented at the following IRB meeting.

A copy of the IRB-approved minutes for each IRB meeting must be distributed to the Institutional Official and NYU Langone Health's Office of General Counsel upon ratification by the IRB.

Minutes of IRB meetings must contain sufficient detail to show:

- The basis for requiring changes in research.
- The basis for disapproving research.
- Justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document.
- The presence of a quorum throughout the meeting, including the presence of one member whose primary concern is in a non-scientific area.
- Attendance at the meetings, including documentation of those members or alternate members who are participating through videoconference or teleconference, and documentation that those attending through videoconferencing or teleconferencing received all pertinent material prior to the meeting and were able to actively and equally participate in all discussions.
- Alternate members attending the meeting and for whom they are substituting.
- Names of consultants present.
- Name of investigators present.
- Names of guests present.
- The initial attendance list shall include those members present at the beginning of the meeting. The minutes will indicate, by name, those members who enter or leave the meeting. The vote on each action will reflect those members present for the vote on that item.
- Business items discussed.
- Continuing education.

- Actions taken by the IRB including those involving full Board review. The IRB must use the minutes to notify IRB members of actions taken through expedited review and those studies that have been determined to be Exempt from IRB review.
- Separate deliberations, actions, and votes for each protocol undergoing initial review, continuing review, or review of modifications by the convened IRB.
- Documentation that the research meets each of the required criteria [45 CFR 46.116(d)] along with protocol-specific information containing justification as to why the IRB considers the research to meet each criterion when approving a consent procedure that does not include or that alters some or all of the required elements of informed consent, or when waiving the requirement to obtain informed consent.
- Documentation that the research meets each of the required criteria [45 CFR 46.117(c)] along with protocol-specific information justifying why the IRB considers the research to meet each criterion when the requirements for written documentation of consent are waived.
- When approving research that involves populations covered by Subparts B, C, or D of 45 CFR 46, the minutes will document the IRB's protocol-specific justifications and findings regarding the determinations stated in the Subparts or the IRB's agreement with the findings and justifications as presented by the investigator on IRB forms.
- The vote on actions, including the number of members voting for, against, and abstaining. Number of those excused, and number of those recused.
- Notations indicating an IRB member's conflicting interest with the research under review, as defined by NYU Langone Health policies (see: Conflicts of Interest).
- and further that the conflicted IRB member was not present during the deliberations or voting on the proposal (and that the quorum was maintained).
- A written summary of the discussion of controversial issues and their resolution.
- Review of additional safeguards to protect vulnerable populations if entered as study subjects when this is not otherwise documented in IRB records.
- For initial and continuing review, the frequency of continuing review of each proposal, as determined by the IRB, including identifications of research that warrants review more often than annually and the basis for that determination.
- Risk level of initial and continuing approved protocols.
- Review of interim reports, e.g. Unanticipated Problems or safety reports; amendments; report of violation/deviations; serious or continuing non-compliance; suspensions/terminations, etc.
- Review of Data and Safety Monitoring Board (DSMB) summary.
- Review of Plans for Data and Safety Monitoring.
- Documentation, as required by 45 CFR 164(i)(2), indicating the approval of a waiver or alteration of the HIPAA Authorization.
- Relevant information provided by consultants will be documented in the minutes or in a report provided by the consultant.
- The rationale for significant risk/non-significant risk device determinations.
- Determinations of conflict of interest management plans and that the IRB found it acceptable.
- Identification of any research for which there is need for verification from sources other than the Principal Investigator that no material changes are made in the research.
- A list of research approved since the last meeting utilizing expedited review procedures.

7.4 MEMBERSHIP ROSTERS

A membership list of IRB members will be maintained and must identify members sufficiently to describe each member's chief anticipated contributions to IRB deliberations. The list must contain the following information about members (IRB Membership Roster).

- Name
- Earned degrees

- Affiliated or non-affiliated status ("non-affiliated" would mean that neither the member him/ herself nor an immediate family member of the member is affiliated with NYUGSoM, NYUGLISoM, or any other part of NYU Langone Health)
- Status as scientist (physician-scientist, other scientist, non-scientist or social behavioral scientist). For purposes of this roster, IRB members with research experience are designated as scientists (including student members). Research experience includes training in research (e.g., doctoral degrees with a research-based thesis) and previous or current conduct of research. Students undergoing training in research fields will be designated as scientists
- Indications of experience, such as board certifications or licenses sufficient to describe each member's chief anticipated contributions to IRB deliberations
- Representative capacities of each IRB member; including naming the IRB member prisoner representative (as required by Subpart C), and naming the IRB members knowledgeable about or experienced in working with children, pregnant women, cognitively impaired individuals, and other vulnerable populations locally involved in research
- Role within the IRB (Chair, Co-Chair, etc.)
- Voting status (Any *ex officio* members are non-voting members)
- Alternate status, including the name of the member he/ she alternates with
- Relationship (e.g., employment) between the individual IRB member and NYU Langone Health

IRB Operations must keep the IRB membership list current.

7.5 DOCUMENTATION OF EXEMPTIONS

Documentation of verified exemptions consists of the reviewer's citation of a specific exemption category and written concurrence that that activity described in the investigator's request for exemption satisfies the conditions of the cited exemption category (see: Categories of Research Permission for Exemptions). The Exempt determination is reported at the next convened IRB meeting and documented in the IRB meeting minutes.

7.6 DOCUMENTATION OF EXPEDITED REVIEWS

IRB records for initial and continuing review of a study by the expedited procedure must include: the specific permissible category; documentation of determination that the activity described by the investigator satisfies all of the criteria for approval under expedited review (see: Categories of Research Eligible for Expedited Review); the approval period; any determinations required by the federal regulations including protocol-specific findings supporting those determinations (such as waiver or alteration of the consent process); and if applicable, the rationale for an expedited reviewer's determination that research appearing on the expedited review list is more than Minimal Risk.

7.7 ACCESS TO IRB RECORDS

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

- Digital IRB records are maintained on password-protected, secure hardware.
- Ordinarily, access to IRB records is limited to the Senior Director, HRP, IRB Chairs, IRB members, IRB Administrators, IRB Operations staff, authorized institutional officials, and officials of federal and state regulatory agencies (OHRP, FDA, etc.). Research investigators are provided reasonable access to files related to their research. Appropriate accreditation bodies are provided access and may recommend additional procedures for maintaining security of IRB records. All other access to IRB records is limited to those who have legitimate need for them, as determined by the IO and Senior Director, HRP.
- Records are accessible for inspection and copying by authorized representatives of regulatory agencies during regular business hours.

- Records may not be removed from the IRB Operations office; however, the IRB Operations staff will provide copies of records for authorized personnel if requested.
- All other access to IRB Study Files is prohibited.

7.8 RECORDS RETENTIONS REQUIREMENTS

"Retention" refers to the storage of records of inactive/closed/terminated/exempt/not-human-subjects-research studies and past IRB Board meeting minutes.

IRB records are stored as described above.

Records pertaining to conducted research must be retained for at least three (3) years after completion of the research. IRB records not associated with research or for protocols cancelled without subject enrollment will be retained at the facility for at least three (3) years after closure.

Physical records associated with closed or terminated studies shall, after the three-(3) year retention period expires, be electronically scanned and thereafter shredded or otherwise destroyed in accordance with institutional policy.

Electronic records must be retained for at least three (3) years on the IRB's current production systems.

7.9 WRITTEN POLICIES AND PROCEDURES

This document details the policies and federal regulations governing research involving human subjects, and further sets forth the requirements for submitting research proposals for review by the NYU Langone Health IRBs.

These *Policies and Procedures* are frequently updated. The Senior Director, HRP will keep the NYU Langone Health research community apprised of any new information that may affect human research protections, including laws, regulations, policies, procedures, and emerging ethical and scientific issues. Such notification may be given via electronic mail, displayed on the NYU Langone Health IRB website and via NYU Langone Health's Office of Science and Research (OSR) web-based newsletter. The *Policies and Procedures* will be available for download through the NYU Langone Health website.

8. IRB REVIEW PROCESS

These procedures and guidelines apply to all research involving human subjects, regardless of sponsorship and performance site, conducted at or under the auspices of NYU Langone Health and at any unaffiliated institutions under the jurisdiction of the NYU Langone Health IRBs.

8.1 HUMAN SUBJECTS RESEARCH DETERMINATION

The Principal Investigator is responsible for making the initial determination as to whether an activity constitutes Human Subjects Research. The Principal Investigator should make this determination based on the definitions of Human Subjects Research (see: Section 3. Definitions). For guidance on whether an activity constitutes Human Subjects Research, Principal Investigators should use the Self-Certification Form for Determining Whether Your Proposed Activity is Research Involving Human Subjects available on the NYU Langone Health HRP's document library online.

The Principal Investigator will be held responsible by the applicable NYU Langone Health IRB to make the proper Human Subjects Research determination. As such, Principal Investigators are urged to request a confirmation from IRB Operations whether an activity constitutes Human Subjects Research. The request may be made verbally, by telephone, via electronic mail or through a formal written communication. All requests must include sufficient documentation of the research activity to support the determination.

Within IRB Operations, determination of whether an activity constitutes Human Subjects Research may be made by experienced members of IRB Operations staff or any member of the IRB. Determinations will analyze whether the activity meets the definitions of "Research" and involves "Human Subjects," using the *Checklist for Human subjects research Determination.* IRB Operations staff will respond to the Principal Investigators' formal requests for determination of Human Subjects Research status in writing. A copy of the submitted materials and determination correspondence will be kept on file by IRB Operations.

8.2 EXEMPT RESEARCH

All research involving human subjects must be approved by the IRB. However, certain categories of research (i.e., "Exempt research") do not require review and approval by a convened IRB. Exempt research is reviewed, determined and approved by an IRB Chair, or designee of the Chair, and is further subject to institutional review. Research cannot be approved by the institution if it has been disapproved by the IRB.

Reviewers will use the *Checklist for Exempt Determination* to determine and document whether or not the research protocol meets the Exempt criteria.

A determination of exemption from IRB review does not equate to an exemption from the HIPAA requirement for Authorization or Waiver of Authorization when the research involves a Covered Entity's protected health information ("PHI"). Researchers who receive an exemption determination but whose research involves PHI must still (1) submit a HIPAA Authorization form (or a request for waiver of HIPAA Authorization), or (2) if applicable, submit a HIPAA form for conducting research involving decedents' information or research using a Limited Data Set. Researchers who wish to review PHI (e.g., medical records) to prepare a research protocol must submit the appropriate HIPAA form for IRB approval.

LIMITATIONS ON RESEARCH SUBJECTS; VULNERABLE POPULATIONS

CHILDREN

Research involving survey or interview procedures or observations of public behavior involving children will not be determined Exempt, except if the research involves observations of public behavior when the investigator does not participate in the activities being observed (see: Child.)

PRISONERS

Research involving prisoners will not be determined Exempt. IRB review is required.

CATEGORIES OF RESEARCH PERMISSIBLE FOR EXEMPTION

The categories of research permissible for exemption are described in the federal regulations at 45 CFR 46.104(d). The IRB Operations staff and IRB members are required to use the *Checklist for Exemption Determination* to make a determination.

Note Regarding Broad Consent:

In the new Common Rule, "Broad Consent" is an (optional) alternative consent process for use **only** for the storage, maintenance, and secondary use of identifiable private information or **identifiable biospecimens** for future, yet-to-be-specified research. To utilize "Broad Consent," the study team and/or the unit/biorepository responsible for the storage of the identifiable data/biospecimens are required to:

- identify the types of research that may be conducted with the data/biospecimens,
- record and track who has agreed to or refused consent, and
- track the terms of consent to determine whether proposed future secondary research use falls within the scope of the identified types of research

IRB PROCESS

At this time, the NYU Langone Health HRP and IRBs will not mandate nor implement the institutional use of Broad Consent, as the tracking requirements may be burdensome. Exemption categories 7 and 8, which rely on Broad Consent, **will not be applied when the IRB reviews Exempt research**.

NYU Langone Health will continue to support study teams seeking subject permission for the collection and storage of identifiable private information/biospecimens for future secondary use research through the following processes:

- Study-specific consent and comprehensive IRB review
- IRB waiver of consent (as eligible) and comprehensive IRB review
- Exemption #4
- De-identification to remove the research activity from Common Rule purview and not require IRB review or consent

Only the IRB may deem a research project to be Exempt from IRB review. Research activities that are not regulated by the FDA (see: FDA Exemptions) in which the only involvement of human subjects will be in one or more of the eight categories found in 45 CFR 46.104(d) (see: 45 CFR 46 Exemptions) are *EXEMPT FROM FEDERAL REGULATIONS, BUT STILL REQUIRE IRB REGISTRATION AND REVIEW*.

FDA EXMPTIONS

The following categories of clinical investigations are not regulated by DHHS or another federal agency and are exempt from the requirements of IRB review prior to commencement of the investigation:

- Emergency use of a Test Article, provided that such emergency use is reported to the IRB within five working days of such use. Any subsequent use of the Test Article at the institution is subject to IRB review [21 CFR 56.104(c)]; and

- Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture [21 CFR 56.104(d)].

HOW TO SUBMIT AN EXTERNAL APPLICATION

Any initial application for Exemption of Human Subjects Research must be submitted electronically via the NYU Langone Health IRB's Research Navigator eSubmission system with the following documentation:

- a summary of the research;

- a description of the research procedures;
- consent documents (if applicable);
- plan for privacy and confidentiality;
- plan for dissemination of findings;
- a copy of the proposal if the research is externally funded, and
- expected date of research completion.

The IRB Chair (or designee) reviews all requests for exemptions and determines whether the request meets the criteria for Exempt research. The IRB Chair may designate an IRB member to review requests for exemptions submitted to the IRB. The IRB Chair selects designees who are qualified to review this category of submission based on their expertise of the protocol content and knowledge of regulations pertaining to research. If a designated reviewer to consider requests for exemptions is not available, the IRB Chair reviews the requests. Individuals involved in making the determination of an IRB Exempt status of a proposed research project cannot be involved in the proposed research, nor can they have any apparent conflict of interest.

The IRB reviewer's determination on the request for Exempt research is documented by the *Exemption Determination Form* to be completed by the reviewer. The IRB reviewer verifies on the form whether the submission meets the definition for "research" or "clinical investigation". If the request meets the definitions of both Human Subject and Research, the reviewer indicates whether the request for exemption was approved or denied, and if approved, the rationale for the determination and exemption category under which it was permitted. Determinations of Exempt studies are communicated to the IRB at the next convened meeting after the approval of exemption is made.

The decision must be communicated in writing to the Principal Investigator and the IRB. Documentation must include the specific categories justifying the exemption.

Investigators will be given feedback as to the qualification of the application for Exempt research status through the eSubmission system. Upon the IRB's completion of the review, the IRB Operations staff will inform the Principal Investigator of the results of the review via electronic mail.

ADDITIONAL PROTECTIONS

Although NYU Langone Health research that is deemed by an IRB to be Exempt research is not covered by the federal regulations, such research is not exempt from NYU Langone Health policies on the responsible conduct of research or the ethical guidelines of the Belmont Report. The individual making the determination of exemption will use the NYU Langone Health *Checklist for Exemption Determination* to determine whether to require additional protections for subjects (including specifics of the informed consent procedures) in keeping with NYU Langone Health institutional policies and/or the ethical guidelines of the Belmont Report.

8.3 EXPEDITED REIVEW OF RESEARCH

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

> (A) some or all of the research appearing on the categorical list below (see: Categories of Research Eligible for Expedited Review) and unless the reviewer determines that the study involves more than Minimal Risk;
>
> (B) minor changes in previously approved research during the period (of one year or less) for which approval is authorized; or

(C) **for new research approved after January 21, 2019**, research for which limited IRB review is a condition of exemption under 45 CFR 46.104(d)(2)(iii), d(3)(i)(c), and (d)(7) and (8).

A minor change is one which, in the judgment of the IRB reviewer, makes no substantial alteration in (i) the level of risks to subjects; (ii) the research design or methodology (e.g., an addition of a procedure which would increase risk to subjects); (iii) the number of subjects enrolled in the research (e.g., increases representing greater than 10%); (iv) the qualifications of the research team; (v) the facilities available to support safe conduct of the research, or (vi) any other change in the research that would otherwise warrant review of the proposed changes by the convened IRB. Adding procedures that are not eligible for expedited review (see: Categories of Research Eligible for Expedited Review) would not be considered a minor change.

Under an expedited review procedure, the review may be carried out by an IRB Chair or by one or more IRB reviewers designated by the IRB Chair. For expedited review purposes, the reviewers designated by the IRB Chair will consist of the Senior Director, HRP, Director of IRB Operations, and the IRB Research Analysts ("Expedited Reviewers"). An IRB Chair may also designate the IRB Vice Chair(s) to assist the designees in review of expedited reviews. The IRB Chair or Senior Director, HRP may appoint other designees from among the members of the IRB when a particular field of expertise is required for an expedited review. Expedited Reviewers at NYUGLISoM are appointed by the NYUGLISoM IRB Chair and Senior Director, HRP among IRB committee members and IRB Operations staff. The Expedited Reviewer(s) may, at their discretion, forward expedited reviews to the IRB Chair or IRB Vice Chair(s) when additional review is needed in order to evaluate Minimal Risk status and determine expedited status. On an annual basis, the IRB Chairs will designate a list of IRB members eligible to conduct expedited review, and IRB Operations will select Expedited Reviewers from that list. IRB members eligible to conduct expedited review must have served on the IRB for at least three (3) months.

When reviewing research under an expedited review procedure, the IRB Chair, or designees, should receive and review all documentation that would normally be submitted for a Full-Board review including the complete protocol, a Continuation review form summarizing the research to date (including modifications and Adverse Events), as applicable, notes from the pre-screening conducted by IRB Operations staff, and the current consent documentation. The IRB Chair or designees shall determine the regulatory criteria for use of such a review procedure by using the *Reviewers Checklist*.

If the research clearly qualifies for expedited review, the reviewer shall conduct the expedited review. If the research does not clearly qualify for expedited review, the reviewer shall refer the application to the IRB for Full Board review at its next convened meeting.

The reviewer(s) conducting the initial or continuing review will complete the appropriate *Institutional Review Board Protocol Review Checklist* in order to determine whether the research meets the expedited procedure criteria and, if so, whether the research meets the regulatory criteria for approval. If the research does not meet the criteria for expedited review, then the reviewer will indicate that the research requires Full Board review by the IRB and the protocol will be placed on the next agenda for an IRB meeting.

For studies approved after January 21, 2019: if the reviewer determines that research appearing on the expedited review list is more than Minimal Risk, he/she will provide documentation of their rationale for the determination.

In reviewing the research, the Expedited Reviewers will follow the Review Procedures described in Review Process and may exercise all of the authorities of the IRB except for disapproval of the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth below.

Expedited Reviewers will indicate approval, required modifications or disapproval within Research Navigator. If modifications are required, the reviewer will inform the Principal Investigator (either via

Research Navigator or via electronic mail. If the modifications are minor, the reviewer(s) may determine if the Principal Investigator has sufficiently addressed the modifications. If the modifications are major and have been reviewed by the IRB Chair or IRB Vice Chair, the reviewer(s) may send the review back to the IRB Chair or Vice Chair (s) for further review. Upon the discretion of the Expedited Reviewer(s) and/ or the IRB Chair or IRB Vice Chair, the protocol may be submitted to the IRB for Full Board review.

In the event that expedited review is carried out by more than one IRB member and the Expedited Reviewers disagree on the resolution of the application, the Senior Director, HRP and/or IRB Chair may make a final determination. Upon the discretion of the Senior Director, HRP or IRB Chair, the protocol will be submitted to the IRB for review.

CATEGORIES OF RESEARCH ELIGIBLE FOR EXPEDITED REVIEW

[63 FR 60364-60367, November 9, 1998]

Inclusion on the list of Research Categories below does not mean that the activities are to be deemed to be of Minimal Risk. Rather, it means that the research activity is eligible for review through the expedited review procedure to determine whether the specific proposed research involves 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 subjects' responses would reasonably place them at risk of criminal or civil liability, or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
- The expedited review procedure may not be used for classified research involving human subjects.
- The standard requirements for informed consent (or waiver, alteration, or exception) apply regardless of the type of review–expedited or convened–utilized by the IRB.

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

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
   (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. However, research on marketed drugs that significantly increase the risks or decrease the acceptability of the risks associated with the use of the drug 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 and/ or approved for marketing, and the medical device is being used in accordance with its cleared/ approved status.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
   - from healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
   - from other adults and children, taking into consideration the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency in which blood samples will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period, and collection may not occur more frequently than 2 times per week.
   - Children are defined in the DHHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." [45 CFR 46.402(a)]

3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples include, *inter alia*: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and sub gingival 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, and (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, such devices must be cleared and/ or 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 include, *inter alia*: (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, and (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

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

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

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

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

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

Note: For categories 8(a) and 8(b) the following applicability criteria apply:

(1) the remaining activities must be Minimal Risk;

(2) if identification of the subjects or their responses will reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal; and

(3) the research may not be classified research. For category 8b, the only applicability criterion is that the research may not be classified research.

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

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

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

If a research protocol has been initially approved through a Full-Board review procedure, the continuing review may not be performed under the expedited review procedure unless such protocol falls within the purview of categories 8 or 9, above. If the protocol was initially targeted for Full Board review but was determined to meet the expedited review criteria outlined above, the reviewer(s) will document that an erroneous review had previously taken place and process the expedited review in accordance with this Policy. The Principal Investigator will be notified of the change in status though electronic mail correspondence.

HOW TO SUBMIT AN EXPEDITED REVIEW

The submission should be made via Research Navigator and include the following documentation:

- a summary of the research;
- description of the research procedures;
- consent documents (if applicable);
- plan for privacy and confidentiality;
- plan for dissemination of findings;
- a copy of the proposal if the research is externally funded;
- a protocol;
- a current CV for each investigator or other study staff listed on the study; and
- a financial disclosure form for each team member listed on the study.

INFORMING THE IRB

All members of the IRB will be apprised of all expedited review approvals by means of the agenda for the next scheduled Full Board meeting. The expedited review approvals will be made available for any optional review at the request of any IRB member.

8.4 CONVENED IRB MEETINGS

Except where eligible for the expedited review procedure, the IRB must review proposed research at convened meetings (also known as "Full-Board" meetings) at which a quorum is present.

SCHEDULE OF IRB MEETINGS

In general, the NYUGSoM IRB meets on the first, second, third and fourth Tuesday of each month (for Boards A, B, C and D, respectively). A special Board E is available to hold ad hoc/emergency meetings; these may be called at any time by an IRB Chair or the Senior Director, HRP and they are held via telephone conference call. The NYUGLISoM IRB has one Board (F) which meets once every two weeks (bi-weekly).

The schedule for the IRB may change as needed due to holidays or lack of quorum.

QUORUM

A quorum consists of a simple majority of the voting membership, including at least one member whose primary concern is in a non-scientific area. If research involving an FDA-regulated article is involved, a licensed physician must be included in the quorum. The IRB Chair, with the assistance of IRB Operations staff, will confirm that an appropriate quorum is present before calling the meeting to order. The IRB Chair will be responsible in ensuring that the IRB meetings remain appropriately convened.

A quorum must be present when voting occurs. The IRB Coordinator takes note of arrivals and departures of all members and notifies the IRB Chair if a quorum is not present. If a quorum is not maintained, the proposal must be tabled or the meeting must be terminated. All members present at a convened meeting have full voting rights, except in the case of a conflict of interest (see IRB Member Conflicts of Interest).

In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting.

While it is preferred that IRB members be physically present at the meeting, if a voting member cannot be physically present at the convened meeting, he/she may be considered present, participate and vote via teleconference or videoconference. In such cases, the member must have received all pertinent material prior to the meeting and must be able to participate actively and equally in all discussions.

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

It is generally expected that at least one IRB member unaffiliated with NYU Langone Health and at least one member who represents the general perspective of subjects will be present at all convened IRB meetings. The same individual can serve in both capacities. Although the IRB may, on occasion, meet without this representation, individuals serving in this capacity must be present for at least 80% of the IRB meetings.

PRE-MEETING DISTRIBUTION OF DOCUMENTS

Review and meeting materials are available electronically via Research Navigator prior to each IRB meeting.

MEETING PROCEDURES

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

The IRB reviews all submissions for initial and continuing review, as well as requests for modifications. The primary and secondary reviewer present an overview of the research (including the study goals, design, procedures, safety procedures, and qualifications of the investigators) and lead the IRB through the completion of the regulatory criteria for approval in the *Institutional Review Board - Protocol Review/Initial Review* checklist appropriate for the type of review (e.g., initial, continuing, amendment).

In order for the research to be approved, it must receive the approval of a majority of those voting members present at the meeting.

At the discretion of the IRB, the Principal Investigator may be invited to the IRB meeting to answer questions about his/her proposed or ongoing research. The Principal Investigator may not be present for the discussion or vote on their research.

IRB Operations is responsible for recording the proceedings and for taking minutes at each IRB meeting.

GUESTS

Guests may be permitted to attend IRB meetings at the discretion of the IRB Chair and the Senior Director, HRP. Guests may not participate in any discussions occurring at the meeting unless requested by the IRB and must sign the IRB's *Confidentiality Agreement* to attend.

PRIMARY REVIEWERS

IRB Operations assigns a primary and secondary reviewer for all protocols requiring initial Full Board review, continuing Full Board review, and for all protocols requiring Full Board review of modifications to previously approved research. When making reviewer assignments, IRB Operations staff will take into consideration the vulnerable populations involved in the research and the scientific or scholarly expertise required to review the research. Such protocols will then be assigned to at least one IRB member who has the appropriate expertise.

If the IRB Operations staff cannot identify a primary reviewer with appropriate expertise, the IRB Chair or the Senior Director, HRP will solicit consultants from NYU Langone Health or the general community with competence in such specialized areas to assist in the review of the issues or protocols requiring appropriate scientific or scholarly expertise beyond or in addition to that available on the IRB (see: Use of Consultants (Outside Reviewers)).

Prior to the convened IRB meeting, each protocol application (including background information, project protocol, and informed consent) is reviewed in depth by the assigned Primary reviewer(s). All other IRB members receive copies of aforementioned with the exception of the protocol and/or investigators brochure. 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, along with the IRB members, then complete the regulatory criteria for approval located in the

Reviewer's Checklists appropriate for the type of review (e.g., initial, continuing, amendment).Both primary reviewers and other IRB members who are not assigned as primary reviewers of proposed studies that require copies of protocols and/or any documentation may access these materials via Research Navigator. Further, upon request, copies of minutes and or study materials can be obtained in hard or electronic format by putting in a request to IRB Operations.

8.5 REVIEW PROCESS

SUBMITTING ELECTRONICALLY TO THE IRB (E-SUBMISSION)

The IRB uses an electronic research administration system made up of several modules and collectively called "Research Navigator," as updated from time to time.

All submissions must be made to the applicable NYU Langone Health IRB via Research Navigator. Initially, a study profile must be completed in the MyStudies module. This module issues the IRB Study Number. Once the MyStudies study profile is complete, any member of the study team may submit the study for initial review. The submission process executes an initial electronic review of the study and makes draft submissions in all of the appropriate OSR review office systems – including the IRB's module, IRB/Research Navigator.

Upon creation of an IRB/Research Navigator submission, IRB Operations is notified electronically and a pre-submission review is conducted by IRB Operations staff. If, upon review of the IRB/Research Navigator submission, all required materials and information appear to have been received, the study's Principal Investigator is notified via email to log into IRB/Research Navigator and confirm through the system through an attestation that the submitted application is complete and accurate, and then formally submit their application to the IRB via electronic signature.

The Principal Investigator's signature is considered valid based on the use of their confidential NYU Langone Health Kerberos ID and password used to log in to the system. It is against NYU Langone Health institutional policy to share a Kerberos password with anyone. During the electronic submission process, the Principal Investigator will be required to submit an attestation to the accuracy of the study submission, the fitness of their study staff, etc.

Initial review submissions also require review and approval of the proposed research by the Principal Investigator's department chair and any of the department chair's delegates "Proxies" they have designated for the review and approval of research. The department chair and Proxies are electronically notified of the initial submission, and may review and approve the study. Final IRB approval is withheld until department chair approval is received.

E-SUBMISSION CONTIGENCY PROCESS

When IRB/Research Navigator is unavailable for an extended time for any reason, one of the following alternative methods for submitting and receiving approval/acknowledgement of a study submission may be used:

MANUAL (WRITTEN) SUBMISSION

If a time-critical submission must be made, a request for manual review of the submission can be made by the study team by contacting IRB Operations and requesting by email the MS Word submission form appropriate to the review type from the IRB. IRB Operations will email this form to the study team for completion. The submission form is then sent back electronically along with electronic copies of all necessary study-related materials for the IRB to review and approve. Any submission-related correspondence including requests for clarification or corrections, and final

approval will be handled via email. A scanned signature of the study's Principal Investigator and department chair may be required to secure review.

If email is also unavailable, the IRB can receive written (printed and manually signed) copies of the necessary documents to review and approve. The IRB will return a written (printed and manually signed) decision letter.

MAKING THE E-SUBMISSION SYSTEM WHOLE

If an alternative submission is utilized, once the IRB/Research Navigator system is back online, IRB Operations will work with the study team to ensure that the electronic submission record for the study incorporates the complete review record, including all materials and issued decision letters along with a public comment as to the 'make-up' nature of the electronic record. This record will be placed on an IRB meeting agenda and reported to the next available Board as necessary. NYU Langone Health's IT department may be called upon to update IRB/Research Navigator submission dates to match the actual dates of submission, review, approval, etc.

DELAYED SUBMISSION

The IRB may ask the study team to delay their submission until such time as the IRB/Research Navigator system is once again available. The final decision is up to the Principal Investigator.

REVIEW PROCESS RESPONSIBILITIES

PRINCIPAL INVESTIGATOR RESPONSIBILITIES

The Principal Investigator is responsible for assuring the informed consent document contains the IRB phone number for subjects to call if they have questions regarding their rights as a volunteer for research. If the IRB has waived the documentation of informed consent, it is the Principal Investigator's responsibility to provide the IRB phone number to the subject by other means.

The Principal Investigator may request copies of the community outreach brochures for distribution to subjects.

IRB COMMITTEE RESPONSIBILITIES

The IRB Committee, Chair, or Executive Committee Member will review each informed consent document to assure that the IRB phone number is included with a statement that the subject may call if they have any questions regarding their rights as a volunteer for research.

IRB OFFICE RESPONSIBILITIES

IRB Operations will assure during the administrative review of proposed NYU Langone Health research that each informed consent document contains the IRB phone number for subjects to call if they have questions regarding their rights as a research volunteer. If the Principal Investigator is requesting a waiver of documentation of informed consent, IRB Operations staff will request information from the Principal Investigator regarding the method of informing the subjects of the IRB phone number for questions.

ADMINISTRATIVE RESPONSIBILITIES

The Director of IRB Operations will evaluate the outreach activities on an annual basis and adjust the program as appropriate.

IRB OPERATIONS PRE-REVIEW

Prior to being placed on an IRB Full Board meeting agenda, new protocol Full Board review applications are screened by the IRB Operations staff for completeness and accuracy, using the appropriate *Pre Review*

Checklist and ensuring regulatory compliance. IRB Operations staff may request additional information and/or request clarification on substantive issues from the Principal Investigator and any assigned primary study contact (such as a research coordinator. Principal Investigators will submit all requests for review, responses to review (etc.) via IRB/Research Navigator unless otherwise instructed.

IRB Operations staff will correct consent form deficiencies (typically limited to editorial changes) and will recommend protocol revisions via Word/ track-changes. IRB Operations staff will check for completeness and accuracy of submissions and further identify the pertinent issues for the IRB Board, and will identify and/or clarify any substantive questions and deficiencies before the protocol is added to an agenda for Full Board review. Changes required by the IRB Operations staff will be incorporated within the applicable IRB/Research Navigator electronic submission record for full review.

Only complete submissions will be placed on the IRB agenda for review. The Principal Investigator and any assigned primary study contact will be informed electronically via the e-Submission system (IRB/Research Navigator) if materials are missing or require substantive changes.

IN-PERSON CONSULTATIONS

In the case of a Principal Investigator who is submitting a protocol for the first time or a Principal Investigator who may not be well-versed in the protocol submission procedures, individualized IRB consultations can be arranged.

Specific questions about the IRB Policies and Procedures, determination of whether a particular protocol is human research or not, and what particular forms are required for a particular study can be submitted in writing to IRB Operations for information and/or clarification. Individual appointments with an IRB Operations staff member can also be arranged and are strongly recommended for first-time submissions.

MEETING MATERIALS RECEIVED FOR THE INITIAL REVIEW OF RESEARCH

Each IRB member will have electronic access via IRB/Research Navigator to the following documentation, as applicable:

- complete IRB protocol application form;
- protocol summary;
- proposed consent / parental permission / assent form(s);
- recruitment materials;
- subject information;
- investigators' curriculum vitae (CV); and
- data collection instruments (including all surveys and questionnaires).

At least one primary reviewer must review:

- any relevant grant applications;
- the sponsor's protocol (when one exists);
- the investigator's brochure (when one exists);
- the DHHS-approved sample informed consent document (when one exists);
- the complete DHHS-approved protocol (when one exists); and
- the Principal Investigator's current CV or other documentation evidencing qualifications.

If an IRB member requires additional information to complete the review, that member may contact the Principal Investigator directly or may contact IRB Operations to make the request of the Principal Investigator.

Protocol reviewers will use the *Reviewer's Checklists* as a guide to completing their review.

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 review the full protocol electronically via IRB/Research Navigator or by contacting IRB Operations.

If an IRB member, consultant, Chair or other reviewer has a conflict of interest in the research undergoing review, he/she/they cannot participate in any IRB action, except to provide information requested by the IRB. It is the IRB member's responsibility to self-identify conflicts of interests (See IRB Member Conflict of Interest).

POSSIBLE IRB ACTIONS TAKEN BY VOTE

IRB members will discuss the study and make determinations regarding category of risk, risk/benefit issues, and whether informed consent procedures are adequate. The IRB will then vote and may take one of the following actions. All actions taken will be recorded in the IRB meeting minutes.

APPROVED

The study is approved as submitted. The research may begin upon receipt of the IRB's written approval and assuming any other required approvals for beginning the research are obtained).

APPROVED WITH CONDITIONS (CONDITIONALLY APPROVED)

The research is approved by the IRB with conditions if, given scope and nature of the conditions, the IRB is able to make all of the determinations required for approval (i.e., approval criteria and any applicable special determinations (e.g., waivers, alterations, vulnerable population determinations, etc.), and based on the assumption that the conditions will be satisfied. Any time the IRB cannot make one or more of the determinations required for approval, the IRB may not issue an approval with conditions for the study.

The IRB may require the following as conditions of its approval of research:

- Confirmation of specific assumptions or understanding on the part of the IRB regarding how the research will be conducted (e.g., confirmation that research excludes children);
- Submission of additional documentation (e.g., certificate of training);
- Precise language changes to the study, consent, or other study documents; or
- Substantive changes to the study, consent, or other study documents along with clearly stated parameters that the changes must satisfy.

When the IRB approves research with conditions, the conditions will be documented in the IRB meeting minutes, and the IRB will notify the Principal Investigator of its approval subject to the conditions being satisfied. The written notification will identify the specific conditions that need to be addressed. The research cannot begin until verification by the IRB that the conditions have been satisfied and IRB final approval letter is sent.
When the convened IRB approves research with conditions, the IRB may designate the IRB Chair (and/or other qualified individual(s)) to review responsive materials from the Principal Investigator and determine that the conditions have been satisfied. If the conditions have not been satisfied, or are only partially satisfied, the responsive materials must be referred to the convened IRB for review.

After verification, the following will be documented in the IRB records and written communication to the Principal Investigator:

- The date when verification was made that all IRB conditions have been satisfied (i.e., the "effective date");
- For initial approval, the date when approval becomes effective (i.e., the date on which the Principal Investigator's response has been accepted as satisfactory); and
- The date by which continuing review must occur.

DEFERRED FOR SUBSTANTIVE ISSUES

Substantive issues regarding the research and /or consent form must be addressed. This action is taken if substantial modification or clarification is required, or insufficient information is provided to judge the protocol application adequately (e.g., the risks and benefits cannot be assessed with the information provided). IRB approval of the proposed research will not be issued by the convened IRB until subsequent review of the requested material that is submitted by the Principal Investigator.

If the application is deferred the following will occur:

- IRB Operations staff informs the Principal Investigator in writing of the IRB's decision, setting forth the IRB's questions and concerns.
- The Principal Investigator's response is sent to IRB Operations.
- In order to receive approval for a deferred protocol, the protocol must be submitted for Full Board IRB review at a subsequent, convened meeting of the same IRB. IRB Operations will provide to the IRB members the Principal Investigator's response, the revised protocol and/or consent with highlighted changes, all original submission materials (inclusive of changes, if any were required), and the previous IRB written decision (relayed to the Principal Investigator by IRB Operations) signed by the Principal Investigator. The deferred protocol is then placed on the agenda for the following meeting.
- The amended protocol application is given full IRB review.
- The outcome of the IRB's deliberations is once again communicated to the Principal Investigator in writing.
- The IRB's determination concerning the subsequent amended submission will be documented in the minutes of that meeting.

DISAPPROVED

Questions and issues surrounding the research are of such a magnitude that the IRB determines approval of the study is unwarranted. If the IRB disapproves a study, the Principal Investigator will be notified in writing of such decision, the reasons for the decision, and be notified of the opportunity to appeal the decision. Approval of a previously disapproved protocol requires full IRB review (*see*: Appeal of IRB Decisions).

APPROVAL IN PRINICPLE [45 CFR 46.118]

There are two circumstances in which the IRB may grant approval required by a sponsoring agency without having reviewed all of the study procedures and consent documents:

- If study procedures are to be developed during the course of the research, but human subjects approval is required by the sponsoring agency.
- If the involvement of human subjects depends on the outcomes of work with animal subjects.

The IRB may then grant approval without having reviewed the, as yet undeveloped, recruitment, consent, and intervention materials. If the proposal is funded, the Principal Investigator must submit such materials for approval at least sixty (60) days before recruiting human subjects into the study, or into any pilot studies or pre-tests. Approval in Principle is granted to satisfy sponsoring agency requirements or to allow investigators to have access to funding to begin aspects of the project that do not involve human subjects.

APPEALS

Should the IRB make a decision the Principal Investigator believes to be unduly restrictive, the investigator may appeal to the full IRB (*see*: Appeal of IRB Decisions).

DETERMINATION OF RISK

Concurrent with the initial and continuing review process, the IRB will make a determination with respect to the risks associated with the research. Risks associated with the research will be classified as either "minimal" or "greater than minimal" based on the "absolute" interpretation of Minimal Risk. The meeting minutes will reflect the IRB's determination regarding risk levels.

PERIOD OF APPROVAL

Concurrent with the initial and continuing review process, the IRB will make a determination with respect to the frequency of review of the research. All protocols will be reviewed by the IRB at intervals appropriate to the IRB's determination of the degree of risk, but no less than once per year. In certain circumstances, a shorter review interval (e.g. bi-annually, quarterly, or after accrual of a specific number of subjects) may be required. The meeting minutes will reflect the IRB's determination regarding review frequency.

REVIEW MORE OFTEN THAN ANNUALLY

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

- Significant risk to research subjects (e.g., death, permanent or long lasting disability or morbidity, severe toxicity) without the possibility of direct benefit to the subjects;
- Involvement of especially vulnerable populations likely to be subject to coercion (e.g., institutionalized psychiatric patients, incarcerated minors); or
- A history of serious or continuing non-compliance on the part of the Principal Investigator.

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

- The probability and magnitude of anticipated risks to subjects;
- The likely medical condition of the proposed subjects;
- The overall qualifications of the Principal Investigator and other members of the research team;
- The specific experience of the Principal Investigator and other members of the research team in conducting similar research;
- The nature and frequency of Adverse Events observed in similar research at this and other institutions;
- The novelty of the research, thereby increasing the possibility of unanticipated Adverse Events;and
- Any other factors that the IRB deems relevant.

In circumstances where the IRB mandates an approval period of less than one year, the IRB may define the review period (1) with a time interval, or (2) in circumstances where a specified number of subjects were studied or enrolled in the study. If a specified number of subjects were studied or enrolled in the study, it is understood that the approval period in no case may exceed one year. Further, the number of subjects studied or enrolled in the study will determine the approval period only when the specified number of subjects were studied or enrolled in the study for less than one year.

INDEPENDENT VERIFICATION REGARDING MATERIALS CHANGES

Protecting the rights and welfare of subjects often requires the IRB to independently verify information about various aspects of the study utilizing sources other than the Principal Investigator. Independent verification includes, but is not limited to:

- Adverse Event reporting;
- information in the scientific literature;
- reports of drug toxicity;
- drug approval status; and

- confirmation that no material changes occurred during the IRB-designated approval period.

The IRB will determine the need for verification from outside sources on a case-by-case basis based upon the following criteria:

- Protocols where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources.
- Protocols conducted by Principal Investigators who have previously failed to comply with federal regulations and/or the requirements or determinations of the IRB.
- Protocols randomly selected for internal audit.
- Any other instance in which the IRB deems verification from outside sources is relevant.

The following factors will also be considered when determining whether or not a study requires independent verification:

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

In making independent verification determinations, 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, review of amendments and/or Unanticipated Problems, or may require such verification at any time during the approval period in the light of new information.

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

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 (a "consent monitor") is required in order to ensure that the approved consent process is being followed and to ensure that subjects are truly giving informed consent.

Such monitoring may be particularly warranted for:

- high risk studies;
- studies that involve particularly complicated procedures or interventions;
- studies involving highly vulnerable populations (e.g., ICU patients, children);
- studies involving study staff with minimal experience in administering consent to potential study subjects; or
- other situations when the IRB has concerns that consent process is not being conducted appropriately.

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

If the IRB determines that consent monitoring is required, the IRB Chair and the Senior Director, HRP will develop a monitoring plan and submit it to the IRB for approval. The consent monitoring may be conducted by IRB Operations staff, IRB members, or another party, either affiliated or unaffiliated with the institution. The Principal Investigator will be notified of the IRB's determination and the reasons for the determination. Arrangements will be made with the Principal Investigator for the monitoring of the consent process for a specified number of subjects. When observing the consent process, the monitor will determine whether the:

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

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

SIGNIFICANT NEW FINDINGS

During the course of research, significant new knowledge or findings about the medication or test article and/or the condition under study may develop. The Principal Investigator must report any significant new findings to the IRB and the IRB will review them with regard to the impact on the subjects' rights and welfare. Since the new knowledge or findings may affect the risks or benefits to subjects or subjects' willingness to continue in the research, the IRB may require, during the ongoing review process, that the Principal Investigator contact the currently enrolled subjects to inform them of the new information. The IRB will communicate this to the Principal Investigator. The informed consent should be updated and the IRB may require that the currently enrolled subjects be re-consented, acknowledging receipt of this new information and for affirming their continued participation. More information can be found in Section 8.8, Reportable New Information.

OTHER COMMITTEE APPROVALS

The Principal Investigator is required to secure the approval of other research committees and institutional committees (if applicable) as may be required by the institution prior to initiation of research activities. For instance, research that involves recruitment of human subjects at NYU Health and Hospitals – Bellevue will require the approval of the BRCC after the study is approved by the NYU Langone Health IRB or their designated IRB of record. In addition, a billing plan approved by NYU Langone Health's CRSU may be required. The Principal Investigator is responsible for submitting the required materials to the appropriate committees required by the institution and securing their approval.

For NYU Langone Health studies, the IRB requires documentation of approval from the following committees (as applicable) prior to issuing IRB approval: Business Conflict of Interest Committee, Institutional Biosafety Committee, ESCRO, and the Radiation Safety Committee. The Senior Director, HRP or designee may serve as a member of all of these ancillary committees to secure timely communication of any modifications resulting in a protocol's review.

In the application for new protocol review, NYU Langone Health Principal Investigators are required to indicate institutional support required for the research, including, as applicable:

- Laboratory
- Medicine
- Pharmacy
- Radiology
- Nuclear Medicine
- Nursing
- Psychiatry
- Outpatient
- Surgery
- Other

For any that are indicated, a letter of support or collaboration must be included and the relevant Department Chair must sign the form.

REPORTING IRB ACTIONS

All IRB actions are communicated directly (electronically via IRB/Research Navigator or by electronic mail) to the Principal Investigator and designated principal contact person for the study within five to seven (5-7) working days of the IRB's determination via a template letter prepared by IRB Operations staff and signed by the Senior Director, HRP. When approving a protocol, the IRB will forward notification of approval along with a copy of the approved consent form. The approval will contain date(s) of the study approval and the expiration date. 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.

A copy of letters to Principal Investigators and other correspondence are maintained by the IRB electronically in IRB/Research Navigator's study files.

The IRB reports its findings and actions to NYU Langone Health in the form of the IRB meeting minutes, which are distributed to the NYU Langone Health IO. Such findings are stored electronically in IRB/Research Navigator.

8.6 CONTINUING REVIEW OF ACTIVE PROTOCOLS

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

APPROVAL PERIOD

Determination of the approval period for a study is made by the IRB on a protocol-by-protocol basis. For each initial and continuing review approval, the IRB will indicate an approval period with an approval expiration date specified. IRB approval is considered to have lapsed at midnight on the expiration date of the approval. For a study approved by a convened IRB, the approval period starts on the date that the IRB conducts its final review of the study; that is, the date that the convened IRB approved the research or the date the convened IRB verified the conditions have been met if the research was approved with conditions. For a study approved under expedited review, the approval period begins on the date the IRB Chair or IRB member(s) designated by the IRB Chair gives final approval to the protocol.

The approval date(s) and approval expiration date are clearly noted on all IRB notifications sent to the Principal Investigator and must be strictly adhered to. Principal Investigators should allow sufficient time for development and review of renewal submissions.

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

No grace periods extending the conduct of research beyond the expiration date of IRB approval will be permitted. Therefore, continuing review and re-approval of research must occur by midnight of the date when IRB approval expires.

Routine expiration reminder notices will be sent electronically either through IRB/Research Navigator or via electronic email to the Principal Investigator and their indicated primary study contact in advance of the approval expiration date and following lapse of IRB approval of a protocol; however, it is the Principal Investigator's responsibility to ensure that the continuing review of ongoing research is approved prior to the expiration date. By federal regulation, no extension past that date can be granted.

IRB approved studies must be conducted in accordance with the terms of the IRB approval until any proposed changes have been reviewed and approved by the IRB.

CONTINUING REVIEW PROCESS

Investigators are responsible for timely submission of continuing review materials. The following must be submitted to the IRB for continuing review:

- the current consent document;
- any newly proposed consent document; and
- *Disclosures of Financial Interest* forms (NYU Langone Health form).

In conducting continuing review of research that is ineligible for expedited review, all IRB members are provided with and review the application and all of the above-referenced material. The primary reviewer and IRB Chair will also receive a copy of the most recent protocol version. At the convened IRB Board meeting, the primary Reviewer will lead the IRB through the completion of the regulatory criteria for approval in the *Reviewer's Checklists*.

IRB Operations staff will attend the convened meetings, and will retrieve any additional related materials the IRB Board members request.

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

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

A new protocol version that has not been previously approved by the IRB will not be accepted at the time of continuing review. Any new protocol/protocol amendment must be submitted through a modification request in IRB/Research Navigator with all accompanying materials and must be approved before reviewing the continuation.

EXPEDITED CONTINUING REVIEW

In conducting a continuing review of research that initially qualified for expedited review, the reviewers will receive all of the above-referenced materials. The reviewer(s) will complete the "*Reviewers Checklist* to determine whether the research meets the criteria allowing continuing review using the expedited procedure and, if so, whether the research continues to meet the regulatory criteria for approval.

Generally, if research did not qualify for expedited review at the time of initial review, it will not qualify for expedited review at the time of continuing review, except in limited circumstances described by expedited review categories (8) and (9) at 63 FR 60364-60367 (see: Categories of Research Eligible for Expedited Review). It is also possible that research activities that previously qualified for expedited review in accordance with 45 CFR 46.110 changed or will change, such that expedited IRB review would no longer be permitted for continuing review.

For new studies submitted and approved by NYU Langone Health IRBs (including those duly authorized by NYU Langone Health) after January 21, 2019, the following applies:

Continuing review of research is not required under federal regulations in the following circumstances [45 CFR 46.109(f)(1]:

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

This does NOT apply to research involving an FDA-regulated test article in a clinical investigation using human subjects, as defined by FDA regulations ("FDA-regulated research"). Continuing review is still required for FDA-regulated research.

An annual notice will be sent to Principal Investigators as a reminder that IRB oversight is still in place, and that modifications, reportable events, and termination/study closure reports must still be submitted to the IRB.

The NYU Langone Health IRB will, however, require continuing review for non-FDA-regulated research if the research meets at least one of the following criteria*:

- The research involves inclusion of vulnerable populations;
- The research involves deception;
- The study has multiple phases/compartments and not all are available/developed at the time of initial review of the protocol;
- Interventional studies involving an FDA-approved drug or device (see Section 8.5, Expedited Research Category 1);
- The research involves sensitive information that presents increased risk to employability, insurability, social stigmatization, criminal or civil liability;
- The research is an interventional study deemed to fall under Expedited Research Category 9).

Does not apply to research reviewed by the IRB in accordance with the limited IRB review process under 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(c), or d(7) or d(8) Continuing review will not be required for those studies.

LAPSE IN IRB APPROVAL

The IRB and Principal Investigators must plan ahead in order to meet required continuing review dates. If the IRB has not reviewed and approved a research study by the end of the approval period specified by the IRB, all research activities must cease, including recruitment and enrollment of subjects, consent,

interventions, interactions, and data collection, unless the IRB concludes that it is in the best interests of individual subjects to continue participation in the research interventions or interactions. This will occur even if the Principal Investigator has provided the continuing review information before the expiration date.

Therefore, Principal Investigators must allow sufficient time for IRB review before the expiration date.

An expiration letter (or electronic mail) will be sent to Principal Investigators by the last date of the approval period.

Failure to submit continuing review information on time is considered non-compliance and will be handled according to the non-compliance policy (see: Non-Compliance).

- If the study is FDA-regulated, the Senior Director, HRP and IRB Chair must follow FDA requirements set forth in 21 CFR 56.108(b)(3) in reaching their decision.

- The sponsoring agency, private sponsor, or other federal agencies must be informed of any lapse of IRB Approval of research via the appropriate institutional business unit (for NYU Langone Health, through the Office of Sponsored Programs Administration).

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

The continuation of research after expiration of IRB approval is a violation of the federal regulations. If the IRB has not reviewed and approved a research study by the study's current expiration date, i.e., IRB approval has expired, research activities must cease. No new subjects may be enrolled in the study. However, the IRB may find that it is in the best interests of individual subjects to continue participating in the research interventions or interactions.

PROCEDURE FOR OBTAING APPROVAL TO CONTINUE SUBJECT PARTICIPATION AFTER LAPSE IN IRB APPROVAL

Once IRB approval lapses for a study, all research activity must cease. However, the Principal Investigator may submit in writing requests to the IRB to approve individual subjects in a study to continue participating in research interventions or interactions if stopping their participation would cause harm. The procedure for obtaining approval to continue subject participation after expiration of IRB approval is as follows:

- The Principal Investigator will submit to the IRB Chair a written list of research subjects for whom stopping of the research would cause harm.
- The IRB Chair will review written requests from investigators who wish to continue research with existing subjects in research procedures.
- The IRB Chair will determine which subjects, if any, may continue with the study. The IRB Chair will further determine the specific procedures that may continue to be performed when ceasing such procedures will harm the subject.

The IRB Chair will either orally communicate the decision to the Principal Investigator(s) or via electronic mail, and in writing.

8.7 MODIFICATION OF AN APPROVED PROTOCOL

Principal Investigators may wish to modify or amend their approved applications. Principal Investigators must seek IRB approval before making any changes in approved research—even though the changes are planned for the period for which IRB approval has already been given. A change may be implemented without IRB approval only when the change is necessary to eliminate an immediate hazard to the subject (in which case the IRB must then be notified at once).

Modifications may be approved if they are within the scope of what the IRB originally authorized. For example, if a researcher wishes to add a population to an existing study, but not alter the study procedures or purpose, a modification request is usually appropriate. Likewise, modifying a procedure without changing the study's purpose or study population may also be appropriate.

Principal Investigators must electronically submit via IRB/Research Navigator all necessary materials necessary to inform the IRB about the changes in the status of their study, including:

- revised protocol application or sponsor's protocol (ifapplicable);
- revised approved consent/parental permission/assent documents (if applicable) or other documentation that would be provided to subjects when such information might relate to their willingness to continueto participate in the study;
- revised or additional recruitment materials;
- any other relevant documents provided by the Principal Investigator; and
- an investigator's current curriculum vitae or other documentation evidencing qualifications (if applicable).

The Principal Investigator must electronically submit all revised materials in Microsoft Word format, noting changes via highlight or "Track Changes".

All changes must be accompanied by a detailed summary of the changes and a rationale (as applicable).

IRB Operations staff will determine whether the proposed changes may be approved through an expedited review process, if the changes are minor, or whether the modification warrants Full Board review. The reviewer(s) using the expedited procedure has the ultimate responsibility to determine that the proposed changes may be approved through the expedited review procedure and, if not, must refer the protocol for Full Board review.

EXPEDITED REVIEW OF PROTOCOL MODIFICATIONS

The IRB may use expedited review procedures to review minor changes in ongoing previously- approved research during the period for which approval is authorized. An expedited review may be carried out by the IRB Chair and/or designee(s) among the IRB. Minor changes/modifications would not include the addition of procedures involving more than Minimal Risk to subjects or changes that do not fall in categories (1)-(7) of research that could be reviewed using the expedited procedure. (See: Categories of Research Eligible for Expedited Review)

The reviewer(s) complete the *Checklist for Amendment Review Determination* to determine whether the modifications meet the criteria allowing review using the expedited procedure, and if so, whether the research with the proposed modifications meets the regulatory criteria for approval.

FULL BOARD REVIEW OF PROTOCOL MODIFICATIONS

When a proposed change in a research study is not minor (e.g., procedures involving increased risk or discomfort are to be added), then the IRB must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB should be promptly informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the subjects' continued welfare.

Major changes/modifications would include the addition of procedures involving more than Minimal Risk to subjects or changes that do not fall in categories (1)-(7) of research that could be reviewed using the expedited procedure (see: Categories of Research Eligible for Expedited Review).

All IRB members review all documents provided electronically by the Principal Investigator.

At the convened meeting, the primary reviewer presents an overview of the modifications and leads the IRB through the completion of the regulatory criteria for approval.

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

CLOSURE OF STUDIES

The completion or termination of the study is a change in activity and must be reported to the IRB. Although subjects will no longer be "at risk" under the study, a final report to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies.

Applications for study closures must be submitted to the IRB electronically via IRB/Research Navigator. The Principal Investigator must submit a final report with the closure application. IRB Operations staff will review the closure application for completeness and will determine how to notify the IRB. Closure applications will be reviewed, noted, and the final report will be included on the next IRB meeting agenda.

8.8 REPORTABLE NEW INFORMATION

DEFINITIONS

ADVERSE EVENT means any physical and psychological harm occurring to subjects during the course of participating in research, whether or not it is related to participation in the research. An Adverse Event can be any unfavorable or unintended event that is temporally related to the research. Examples of Adverse Events include: abnormal laboratory findings, nightmares, broken wrist, upper respiratory tract infection, nausea and vomiting, and other symptoms or diseases. Although Adverse Events occur most commonly in the context of biomedical research, Adverse Events can occur in the context of social and behavioral research.

UNANTICIPATED PROBLEM INVOLVING RISKS TO SUBJECTS OR OTHERS **(***UNANTICIPATED PROBLEM)* means any event, incident, experience, outcome, or new information that (1) was unexpected (in terms of nature, severity, or frequency) given the information provided in research-related documents and characteristics of the subject population being studied; and (2) is related or possibly related to participation in the research; and (3) suggests that the research caused harm to subjects or others or places subjects or others at increased risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

REPORTABLE NEW INFORMATION ("RNI") also known as, Reportable Events, for purposes of this Policy, refers to any new information, unanticipated events or unintentional mistakes that arise during the conduct of Human Subject Research that may impact the conduct of an IRB-approved, Human Subjects Research study or the safety and welfare of the participants in that study.

REPORTABLE NEW INFORMATION (RNI)

Federal regulations require that institutions engaging in human subjects research have written procedures to ensure investigators report certain events to the IRB. This section of the policy and procedures defines who is required to report events, what events require prompt reporting, when to report, and how to report to the

NYU Langone Health IRB. The policy applies to all research studies that are overseen by the NYU Langone Health IRB.

WHO IS RESPONSIBLE FOR REPORTING EVENTS

During the course of a research study, unexpected events or unintentional mistakes in following the IRB-approved protocol may occur that could impact human subjects or others involved in the research. It is the Principal Investigator's responsibility to review events and determine whether an event fits the reporting requirements and categories below. **Events that do not fit into one of the categories below do not need to be submitted to the IRB. The Principal Investigator may delegate reporting of the event to anyone on the study team but is ultimately responsible for ensuring RNIs are submitted to the IRB.**

WHAT EVENTS REQUIRE REPORTING

RNIs that require reporting to the IRB are typically unanticipated, related, or probably related to the research and may increase risk of harm or present actual harm to subjects. Other RNIs outlined below may need to be reported to the IRB in order for the IRB to determine whether subject safety or rights have been impacted or whether there has been non-compliance.

Events can occur which are unexpected and result in new circumstances that increased the risk of harm to subjects without directly harming them. The event may have presented unanticipated risks to others (e.g., the sexual partners of the subjects, individuals the subject may come in contact with, family members, research personnel, etc.) in addition to the subjects. In each case, even if the event did not cause any detectable harm or adverse effect to subjects or others, they nevertheless may be reportable as an RNI and should be promptly reported under this Policy.

The following categories of events are considered reportable and require a submission to the IRB using the Reportable New Information e-submission form found in Research Navigator. A Modification submission in IRB/Research Navigator may also be required.

1. New or Increased Risk

Information arising from the study that indicates a new or increased risk or safety issue. For example:

- New information (e.g., an interim analysis, safety monitoring report, publication in the literature, sponsor report, or investigator finding) indicates an increase in the frequency or magnitude of a previously known risk or uncovers a new risk
- An investigator realizes that subjects have accidentally been given study drug at a higher dose than was approved by the IRB. While no side effects were reported, the increase in dosage placed the subjects at potential risk of harm
- An investigator brochure, package insert, or device labeling is revised to indicate an increase in the frequency or magnitude of a previously known risk, or to describe a new risk
- Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol
- Protocol violation that harmed subjects or others, or that indicates subjects or others might be at increased risk of harm
- Complaint of a subject that indicates subjects or others might be at increased risk of harm or at risk of a new harm
- Any changes significantly affecting the conduct of the research

2. Unexpected Harm to a Subject or Other Individual

Any harm experienced by a subject or other individual(s) that, in the opinion of the investigator, is

unexpected and related or possibly related to the research procedures. Harms can include psychological, economic, legal, and other non-physical harms.

- A harm is "unexpected" when its specificity or severity is inconsistent with risk information previously reviewed and approved by the IRB in terms of nature, severity, frequency, and characteristics of the study population
- A harm is "probably related" to the research procedures if, in the opinion of the investigator, the research procedures more likely than not caused the harm

Note: An event that is expected, as identified in the study documentation, but is occurring at greater frequency or severity, as determined by the investigator's and/or sponsor's assessment, may be considered unexpected and should be reported to the IRB as an RNI.

An event that is determined to be unrelated to the study, or are directly related to the subject population's disease, should not be submitted to the IRB.

Examples of harm include:

a. Death of a Research Subject. Investigators are required to report deaths of research participants to the IRB if the death was unanticipated and related or probably related to participation in the study.
   - The investigator should contact IRB Operations as soon as possible via phone or email.
   - Depending on the circumstances, the IRB may need to take immediate action to minimize further harm to subjects, such as halting the enrollment of additional subjects or suspending approval of the research.
   - Formal notification to the IRB of the event is still required and accomplished through a RNI submission under the applicable study in IRB/Research Navigator.

b. Adverse Events. Adverse Events, which typically occur in biomedical research, can also occur in the context of social and behavioral research. Only Unanticipated Adverse Events that are related to the research need to be reported to the IRB. As described above, RNI includes events that may increase risks or cause harm. Adverse Events occur most commonly in the context of biomedical research.

c. Unanticipated Adverse Device Effect. Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device must be reported to the IRB if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

3. Non-Compliance

Non-compliance with federal regulations governing human research, NYU Langone Health's HRP policies, or with IRB requirements or determinations, or allegations of such non-compliance.

4. Audits

External audits, inspections, or inquiries by a federal agency and any resulting reports (e.g., FDA Form 483).

5. Reports

Written reports of study monitors, reports to/from a study sponsor or other information that indicates a change to the risks or potential benefits of the research. For example:

- sponsor-imposed suspension of the research based on risk;
- an interim analysis or safety monitoring report indicates that frequency or magnitude of harms or benefits may be different than those initially presented to the IRB; or
- a paper is published from another study that shows that the risks or potential benefits of the research may be different than initially presented to the IRB.

6. Researcher Error

Failure to follow the protocol due to the action or inaction of the investigator or research staff.

7. Breach of Confidentiality

Breach of subject or patient confidentiality, data breach, or data incident. Any unauthorized disclosure of subject's personally identifiable information. PLEASE NOTE: Potential breaches of confidentiality that involve protected health information (PHI) must also be reported promptly to the HIPAA Privacy Officer.

8. Unreviewed Change

Any change in the IRB-approved study protocol that was taken without prior IRB review to eliminate immediate hazard to subjects must be reported. This would include protocol violations and deviations. For clarity, the NYU Langone Health IRBs do not require reporting of minor unintentional or intentional changes to the IRB-approved protocol unless the deviation was made due to concerns of subject safety or rises to the level of a protocol deviation.

A protocol violation refers to an accidental or unintentional change to the IRB-approved protocol that harmed subjects or others, or that indicates subjects or others may be at increased risk of harm. Examples: subject received the wrong dose of study medication.

9. Incarceration

Investigators must report to the IRB when a subject who is enrolled in a study that is not IRB-approved to involve prisoners becomes incarcerated and the study team plans to continue study activities with prisoners while incarcerated.

10. Complaint

Complaints made by a subject that are related to the study and either indicate increased risk and/or that cannot be resolved by the research team must be reported.

11. Suspension or Termination

Principal Investigators must report premature suspension or termination of the research by the sponsor, investigator, or institution.

Note: Principal Investigator Holds must be reported to the IRB as referenced under Section 12.3, Suspension or Termination of a Study. A Hold is not considered to be a reportable event under this Policy and thus should not be handled under this Section 8.8: Reportable New Information. However, the event that led to the Hold, if an RNI, should be reported to the IRB in accordance with this Section.

WHEN TO REPORT EVENTS

All reportable events, meaning those that are **unexpected** and meet the category of events above, must be reported to the NYU Langone Health IRB immediately but no later than ten (10) calendar days of becoming aware of the event.

If the reportable event is an NYU Langone subject's death, the Principal Investigator should report such event to the IRB immediately but no later than five (5) calendar days of becoming aware, whether or not causality (relatedness to the research) has been determined.

If an event requires immediate intervention to prevent serious harm to subjects or others, the investigator may act accordingly to prevent harm and then must report the event and all interventions taken within five (5) days.

Investigators must report all other possible RNIs occurring at the local research site and non-local research sites to the IRB as soon as possible but no later than ten (10) calendar days from the date of the event or from the date the investigator is notified of the event.

The IRB will accept other reports when the Principal Investigator is unsure whether the event should be reported. The Principal Investigator should first contact IRB Operations by email or telephone to determine if the reporting is necessary under this Policy.

Events that do not meet the above criteria should be summarized and reported to the IRB at the time of continuing review.

PROCEDURES FOR REPORTING EVENTS TO IRB

Investigator and/or Study staff must report the RNIs electronically using NYU Langone Health's Research Navigator system. Using the IRB electronic submission form titled *Reportable New Information,* the study team will be required to report all events described in the subsection What Events Require Reporting.

Note: The RNAV system attempts to simplify reporting to the IRB by only having one reporting category, "Reportable New Information". When investigators submit a reportable event in the RNAV system, they must select the type of reportable event (as noted above under What Events Require Reporting). The RNI form allows for an investigator to submit a single submission to be attached to multiple protocols. For example, if the FDA issued a new black box warning for a medication that is being used in multiple research protocols by an investigator, the investigator could submit one new RNI submission and link this report to all of his/her protocols that are using that medication).

IRB REVIEW OF REPORTABLE NEW INFORMATION

Upon receipt, the event will be assessed to determine the level of review required. RNIs will be reviewed by an IRB Senior Manager who may either make a determination as a designee of the IRB Chair or may determine that the event must be referred to a convened IRB.

RNI REVIEW BY CONVENED IRB

If the RNI is referred to a convened IRB, all IRB members are provided a copy of the RNI and supporting documents. The convened IRB may require the Principal Investigator to provide more detailed information, or require the study sponsor, coordinating center, or DSMB/DMC to do so.

Determinations

The convened IRB will make findings and recommendations based on the following considerations:

1. Whether the reported event is an Unanticipated Problem according to the definition in this Policy;

2. Whether the reported is non-compliance in accordance with the definition in this Policy; or

3. Whether the event is not non-compliance and not an Unanticipated Problem, but is still a reportable event requiring action.

Actions

If the convened IRB determines that the event is neither an Unanticipated Problem nor non-compliance, the IRB may determine any of the following actions are needed:

1. No further action;
2. Required modifications to the protocol;
3. Revisions to the continuing review timetable;
4. Modification of the consent process;
5. Modifications to the consent document;
6. Providing additional information to current subjects (e.g. whenever the information may relate to the subject's willingness to continue participation);
7. Providing additional information to past subjects;
8. Requiring additional training of the Principal Investigator and/or study staff; and/or
10. Other actions appropriate for the local context.

If the convened IRB determines that the event represents an Unanticipated Problem and/or non-compliance, the IRB may recommend any of the following actions:

1. Required modifications to the protocol;
2. Modification of the information disclosed to subjects during the consent process;
3. Providing additional information to current subjects (This must be done whenever the information may relate to the subject's willingness to continue participation);
4. Providing additional information to past subjects;
5. Requiring current subjects to re-consent to participation;
6. Alteration of the frequency of continuing review;
7. Observation of the research or the consent process;
8. Required additional training of the Principal Investigator and/or study staff;
9. Notification to investigators at other sites;
10. Termination or suspension of the research according to Section 12: Complaints, Non-Compliance, and Suspension or Termination of IRB Approval of Research;
11. Obtaining additional information;
12. Referral to other organizational entities (e.g., Office of General Counsel, risk management, Institutional Official); and/or
13. Other actions appropriate for the local context.

Any actions in response to the reported event may include, but not be limited to, suspension or termination of IRB approval. See Section 12, Complaints, Non-Compliance, and Suspension or Termination of IRB Approval of Research.

If the convened IRB finds that further reporting of the RNI to institutional and/or federal officials is necessary, the procedures in Section 13. Reporting to Regulatory Agencies and Institutional Officials, will be followed.

The results of the convened IRB review are recorded in the IRB meeting minutes, protocol record, communicated to the Principal Investigator and referred to IRB Operations to be handled according the reporting procedures (see: Section 13: Reporting to Regulatory Agencies and Institutional Officials).

8.9 FURTHER REVIEW/APPROVAL OF IRB ACTIONS BY OTHERS WITHIN THE INSTITUTION

Research that has been approved by the IRB may be subject to further appropriate review and approval or disapproval by officials of the institution; however, those officials may not authorize research if it has been not been approved by the IRB [45 CFR 46.112]. There are no required institutional reviews after the IRB grants its approval, but the institution reserves the right to subject research reviewed by the IRB to further review.

8.10 APPEALS OF IRB DECISIONS

The Principal Investigator may request that the IRB reconsider a decision in the following circumstances: (1) the IRB has disapproved a submission, or (2) the IRB has made a decision that the Principal Investigator believes is unduly restrictive upon a research project. Before submitting a formal appeal, the Principal Investigator may first discuss the matter with the IRB Chair and/or the Senior Director, HRP.

If the issue cannot be resolved satisfactorily through discussion, the Principal Investigator may submit a written appeal to the Senior Director, HRP. The Principal Investigator must provide substantive new information that was not previously presented that could affect the IRB's decision, and explain the reasons for the appeal.

The appeal should be submitted through the IRB system. The Senior Director, HRP will discuss with the IRB Chair whether the appeal warrants review by a convened Board or can be decided by the Chair. If the convened Board hears an appeal, the Principal Investigator should be prepared to attend the meeting to address issues raised by the Board. The IRB will notify the Principal Investigator of the determination. No further appeal of a decision will be permitted unless the Principal Investigator provides the IRB with additional new substantive information not previously provided.

8.11 SPONSORED RESEARCH CONTRACTS

NYU Langone Health requires that all of its funded human subjects research must be reviewed and approved by the NYU Langone Health IRB, or another duly authorized IRB. Proposals to be submitted for external funding by a non-industry funding source are submitted through Research Navigator to NYU Langone Health's Sponsored Programs Administration (SPA). SPA office staff review the submission to determine if the "human subjects" box is checked indicating that human subjects research is included in the proposal. If the human subjects' box is not checked, the SPA staff review the abstract or the statement of work to determine if the project involves human subjects and the box should be checked. If necessary, SPA office staff will contact IRB Operations (or other affected compliance offices) to determine appropriate follow up action. If it is determined that the proposed research involves human subjects, the Principal Investigator is advised to submit the proposal to IRB Operations.

Contracts covering the provision to NYU Langone Health of financial and/or drug or device support for clinical research will be reviewed and negotiated by OSR Contracts consistent with NYU Langone Health policies and practices, including to address the following concepts, as applicable:

- consistency between the contract(s) and the informed consent form reviewed by the IRB;
- assurances that the NYU Langone Health Principal Investigator will follow the protocol, applicable regulations, and ethical standards;
- clarification on which entity, if any, will be responsible for research-related injuries;
- whether the counterparty will monitor the conduct of the research, and whether the contract includes an assurance that if the study monitor uncovers information that could affect the safety of subjects or their willingness to continue participation, influence the conduct of the study, or alter the IRB's approval to continue the study, the counterparty will make sure that the information is communicated to the Principal Investigator and IRB;

- whether the contract includes an assurance that, if the counterparty discovers results that could affect the safety or medical care of study subjects, it will make sure the Principal Investigator and IRB are notified.

8.12 IRB FEE POLICY AND SCHEDULE

A fee will be required for all NYU Langone Health IRB reviews of new protocols, continuing reviews, and protocol amendments, and for review of Modifications and RNIs for industry sponsored studies .

IRB fees are applied even if subjects are never enrolled, the study terminates before milestones are met, expenditures exceed revenue, or a contract is never finalized.

These fees should be included as a line item in the budget of the formal contract as an upfront and non-refundable item negotiated through the responsible department of the institution (in the case of NYU Langone Health industry-funded clinical research, the Clinical Research Support Unit).

8.13 THE RIGHTS OF RESEARCH SUBJECTS

It is the policy of NYU Langone Health HRP to provide information to the community regarding the rights of research volunteers who participate in NYU Langone Health research.

- The HRP will require that a telephone contact number be provided to each subject consented to participate in research. The contact number should appear on every informed consent document along with a statement about whom the subject may contact regarding questions (i.e., if the subject needs additional information), concerns, or complaints regarding his/her rights as a research subject. This information is included in the NYU Langone Health Human Research *Informed Consent template* in the section entitled Contact Person(s).

- The NYUGSoM IRB has provided the community with a section on the NYUGSoM IRB website that provides potential and current research subjects additional information regarding participation in a research study. The website is located at https://med.nyu.edu/research/office-science-research/clinical-research/prospective-current-study-participants

- The IRB maintains a mechanism to receive complaints from subjects or others in a confidential manner.

- A brochure for research volunteers is available entitled, "Thinking About Enrolling in a Clinical Trial?" found in Resources for Prospective and Current Study Participants and includes the following:
    - a lay definition of research and research personnel
    - a discussion of potential risks and benefits of research
    - what information should be made available in an informed consent
    - research Participant's Bill of Rights
    - who to contact for questions concerning participation in a research study
- Representatives from the NYUGSoM IRB participate in community outreach activities such as speaking engagements to patient support groups.

- The NYUGSoM IRB actively recruits community members for service on the panels through community outreach programs and organizations.

- The NYUGSoM IRB and Clinical and Translational Science Institute (CTSI) Research Participant Advocates respond to inquiries, complaints, and requests for information from patients, research subjects, and community members.

- The Patient Advisory Council for Research (PACR), which consists of patients from NYU Langone Health, provides regular feedback on the following: (1) ways to make research

projects more patient-friendly, (2) how best to engage patients in clinical trials and health research, (3) how best to advertise studies, and (4) concerns and potential challenges around study recruitment and retention.

The applicable Senior Director, HRP and IO will evaluate the effectiveness and impact of the NYU Langone Health IRBs' outreach activities on an annual basis or more often. The evaluation will entail both auditing of the informed consent process, interviewing and surveying research subjects that have been enrolled in research studies.

The oversight function of the outreach program will become part of a continuous Quality Improvement program that will support the maintenance of higher standards of human subjects protections. In order to formally evaluate its outreach activities, the IRB Associate Director will determine:

- the specific community outreach activities being used
- whether or not these community outreach activities have an evaluative component, and if so what, ifany, changes in the outreach activities have resulted from these evaluations

The Director of IRB Operations in collaboration with the CTSI's Community Engagement and Population Health Research program (CEPHR) will administer surveys annually to determine the adequacy of outreach activities. The survey will assess:

- the scope, the content and the adequacy of outreach activities and resources
- whether the research community is using the NYU Langone Health IRB website resource for prospective and current research subjects
- whether the NYU Langone Health research community is using other educational materials to inform prospective subjects about their rights and welfare as research subjects
- whether additional resources are needed to improve subject outreach activities

The results of the survey will be used to establish both the adequacy of current outreach activities and any additional resources that may be needed to meet the needs of the NYU Langone Health research community regarding subject outreach.

9. CRITERIA FOR IRB APPROVAL OF RESEARCH

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

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

- Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by [45 CFR §46.116].
- Informed consent will be appropriately documented, in accordance with, and to the extent required by [45 CFR §46.117].
- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

For purposes of conducting the limited IRB review, the IRB need not make the determinations bulleted above, and shall make the following determinations:

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

9.1. RISK/BENEFIT ASSESSMENT

One of the major responsibilities of the IRB is to conduct a risk/benefit assessment of the proposed human subjects research. The goal of the assessment is to ensure that the risks to research subjects posed by participation in the research are justified by the anticipated benefits to the subjects or society. Toward that end, the IRB must:

- judge whether the anticipated benefit, either of new knowledge or of improved health for the research subjects, justifies asking any person to undertake the risks; and
- disapprove research in which the risks are judged unreasonable in relation to the anticipated benefits.

The assessment of the risks and benefits of proposed research involves a series of steps:

- Identify the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research.
- Determine whether the risks will be minimized to the extent possible.
- Identify the probable benefits to be derived from the research.
- Determine whether the risks are reasonable in relation to the benefits to subjects, if any, and assess the importance of the knowledge to be gained.
- Ensure that potential subjects will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits.

Risks to subjects are minimized:

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

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

- In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research—as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research.
- The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

SCIENTIFIC MERIT

In order to assess the risks and benefits of the proposed research, the IRB must determine that the science is adequate to provide sufficient benefit to justify the risks, including:

- the research uses procedures consistent with sound research design;
- the research design is sound enough to reasonably expect the research to answer its proposed question; and
- the knowledge expected to result from this research is sufficiently important to justify the risk.

For research that is funded externally or is internally funded (such as through local research award programs) the IRB may take into account that the research will be going through a peer review process.

For departments that conduct scientific merit review, departmental scientific review is documented by the signature of the administrative official responsible for the Principal Investigator's research unit on new protocol applications. In cases where the proposed research is not funded and there is no departmental scientific review, the IRB relies on the knowledge and disciplinary expertise of its members and alternates or consults with other researchers on or off campus for scientific merit review.

The IRB will require documentation demonstrating that the following questions where considered during the scientific review:

- Does the research uses procedures consistent with sound research design?
- Is the research design sound enough to reasonably expect the research to answer its proposed question?

For research that is subject to ICH-GCP guideline (E6):

- Policies and procedures include the evaluation of the available nonclinical and clinical information on an investigational product is adequate to support the proposed clinical trial.
- Clinical trials must be scientifically sound and described in a clear, detailed protocol.

OTHER CONSIDERATIONS

In assessing the benefits of the research, the IRB must also review:

- the qualifications of the research team, including their technical and scientific expertise, as well as their knowledge and understanding of their obligation to protect the rights and welfare of research subjects; and
- the adequacy of the resources necessary for human research protection, care of research subjects, and safety during the conduct of the research.

9.2. SELECTION OF SUBJECTS IS EQUITABLE

The IRB will review the inclusion/exclusion criteria for the research to ensure equitable selection of subjects. In making this assessment the IRB takes into account the purposes of the research and the setting in which the research will be conducted, and is particularly cognizant of the special problems of research

involving vulnerable populations, such as children, prisoners, fetuses, pregnant women, human in vitro fertilization, persons who are cognitively impaired, or persons who are economically or educationally disadvantaged (see: Vulnerable Populations).

RECRUITMENT OF SUBJECTS

The Principal Investigator will provide the IRB with all recruiting materials to be used in identifying subjects for the IRB's review, including:

- the information contained in the advertisement (including web-based sites)
- the mode of its communication
- the final copy of printed advertisements
- the final audio/video taped advertisements

The IRB must approve any and all advertisements prior to posting and/or distribution. The advertising material must be accurate, should not be coercive or unduly optimistic, or create undue influence to the subject to participate. The content of the advertisement should be limited to the information the prospective subjects need to determine their eligibility and interest in participation.

The IRB will review:

- the information contained in the advertisement
- the mode of its communication
- the final copy of printed advertisements
- the final audio/video taped advertisements

The IRB reviews advertising to ensure that advertisements do not:

- make claims, either explicitly or implicitly, that the drug, biologic or device is safe or effective for the purposes under investigation;
- state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol;
- make claims, either explicitly or implicitly, that the test article is known to be equivalent or superior to any other drug, biologic or device;
- use terms, such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational;
- promise "free medical treatment," when the intent is only to say subjects would not be charged for taking part in the investigation;
- include exculpatory language; and
- emphasize the payment or the amount to be paid, by such means as larger or bold type.

The IRB determines that advertisements are limited to the information prospective subjects need to determine their eligibility and interest, such as:

- the name and address of the clinical investigator or research facility;
- the condition under study or the purpose of the research;
- in summary form, the criteria that would be used to determine eligibility for the study;
- a brief list of participation benefits (if any);
- the time or other commitment required of the subjects;
- the location of the research and the person or office to contact for further information;
- a clear statement that this is research and not treatment;
- a brief list of potential benefits (e.g. no cost of health exam); and

- advertisements will not include reimbursement/compensation for participation in a trial offered by a sponsor to involve a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

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

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

9.3. INFORMED CONSENT

The IRB will ensure that informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116 and 21 CFR 50.20. In addition, the IRB will ensure that informed consent will be appropriately documented in accordance with, and to the extent required by [45 CFR 46.117] and [21 CFR 50.27].

For detailed IRB policies on informed consent (see: Section 10: Informed Consent).

9.4. DATA SAFETY MONITORING

The IRB will review the data safety monitoring plan for protocols involving more than minimal risk during initial review and at the time of continuing review. The initial plan submitted to the IRB should describe the procedures for safety monitoring, reporting of RNIs involving risks to subjects or others, descriptions of interim safety reviews and the procedures planned for transmitting the results to the IRB. This description should include information regarding an independent Data and Safety Monitoring Board (DSMB), if one exists, or an explanation why an independent data safety monitor is not necessary.

The IRB determines that the safety monitoring plan makes adequate provision for monitoring the reactions of subjects and the collection of data to ensure the safety of subjects. The overall elements of the monitoring plan may vary depending on the potential risks, complexity, and nature of the research study. The method and degree of monitoring needed is related to the degree of risk involved.

Monitoring may be conducted in various ways or by various individuals or groups, depending on the size and scope of the research effort. These exist on a continuum from monitoring by the Principal Investigator in a small, low risk study to the establishment of an independent DSMB for a large phase III clinical trial.

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

- Monitoring is commensurate with the nature, complexity, size and risk involved.
- Monitoring is timely. Frequency should commensurate with risk. Conclusions are reported to the IRB.
- For low risk studies, continuous, close monitoring by the study Principal Investigator or an independent individual may be an adequate and appropriate format for monitoring, with prompt reporting of problems to the IRB, study sponsor and regulatory bodies as appropriate.
- For studies using only an individual safety monitor, the plan must include:
    - parameters to be assessed;

  - mechanism to assess the critical efficacy endpoints at intervals in order to determine when to continue, modify, or stop a study;
  - frequency of monitoring; and
  - procedures for reporting to the IRB.
- For studies using a DSMB, the plan must include:
  - the name of the DSMB;
  - where appropriate, is independent from the study sponsor;
  - availability of written reports;
  - composition of the monitoring group (if a group is to be used): the DSMB should include experts in all scientific disciplines needed to interpret the data and ensure patient safety. Clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease and treatment under study should be part of the monitoring group or be available if warranted;
  - frequency and content of meeting reports; and
  - the frequency and character of monitoring meetings (e.g., open or closed, public or private).

In general, it is desirable for a DSMB to be established by the study regulatory sponsor for research that is blinded, involves multiple sites, involves vulnerable subjects, or employs high-risk interventions. For some studies, the National Institutes of Health (NIH) require a DSMB. The IRB has the authority to require a DSMB as a condition for approval of research where it determines that such monitoring is needed. When DSMBs are utilized, IRBs conducting continuing review of research may rely on a current statement from the DSMB indicating that it has and will continue to review study-wide 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.

9.5. PRIVACY AND CONFIDENTIALITY

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

DEFINITIONS

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

CONFIDENTIALITY means the methods used to ensure that information obtained by researchers about their subjects is not improperly divulged.

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

IDENTIFIABLE INFORMATION means information where the identity of the subject is or may readily be ascertained by the Principal Investigator or associated with the information.

PRIVACY

The IRB must determine whether the activities in the research constitute a violation of privacy. In order to make that determination, the IRB must obtain information regarding how the investigators obtain access to subjects or subjects' information and the subjects expectations of privacy in the situation.

The Principal Investigator must have appropriate authorization to access the subjects or the subjects' information. In developing strategies for the protection of subjects' privacy, consideration should be given to:

- methods used to identify and contact potential subjects;
- settings in which an individual will be interacting with an investigator;
- appropriateness of all personnel present for research activities;
- methods used to obtain information about subjects and the nature of the requested information;
- information that is obtained about individuals other than the "target subjects," and whether such individuals meet the regulatory definition of "human participant" (e.g., a subject provides information about a family member for a survey); and
- how to access the minimum amount of information necessary to complete the study.

CONFIDENTIALITY

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

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

- about subjects;
- about individuals who may be recruited to participate in studies;
- the use of personally identifiable records; and
- the methods to protect the confidentiality of research data.

The Principal Investigator should provide the information regarding the privacy and confidentiality of research subjects at the time of initial review through the completion of the protocol application, any necessary Health Insurance Portability and Accountability Act (HIPAA) authorization forms, research protocol, and/or other submitted, applicable materials. The IRB will review all information received from the Principal Investigator and determine whether or not the privacy and confidentiality of research subjects is sufficiently protected. In some cases, the IRB may also require that a Certificate of Confidentiality be obtained to additionally protect research data (see: Certificate of Confidentiality).

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

9.6. VULNERABLE POPULATIONS

If vulnerable populations are likely to be involved in the research, at the time of initial review, the IRB will consider the scientific and ethical reasons for including vulnerable subjects in the research and will determine if appropriate additional safeguards are in place to protect the rights and welfare of such subjects (e.g., persons with diminished autonomy) (see: Section 11: Vulnerable Populations).

9.7. SPECIAL REQUIREMENTS FOR RESEARCH FUNDED BY THE DEPARTMENT OF DEFENSE

If the research is supported by the United States Department of Defense (DoD), (1) it must be reviewed and conducted in compliance with the Common Rule, adopted at part 219 of title 32 CFR, and FDA regulations on human subjects research, and (2) also must comport with DoD Instruction (DoDI) 3216.02, "Protection of Human Subjects and Adherence to Ethical Standards in DoD-Conducted and Supported Research," (last updated April 15, 2020) including all references included therein. These additional requirements apply to any human subjects research that is conducted, reviewed, approved, overseen, supported, managed or otherwise contractually subject to applicable regulations by DoD, or that uses DoD property, facility or assets ("DoD-Supported Research").

Excerpts and summaries of DoDI 3216.02 requirements are included below for ease of reference, but in the event of any conflict between provisions of this policy and any regulations or guidance provided by the DoD or its components, such regulations or guidance shall control. The complete DoDI 3216.02 is available at [https://www.esd.whs.mil/Portals/54/Documents/DD/issuances/dodi/321602p.pdf] and is incorporated by reference in full into this Policy.

Following IRB review, non-Exempt research protocols covered by these requirements must also be reviewed administratively by the relevant DoD Human Research Protections official (HRPO) before the activities that involve human subjects can begin (e.g., human subject recruitment and data collection) [DoDI 3216.02, section 3, para 3.6.b(6).]. No such research may begin until such approval by DoD has been received in writing.

MINIMAL RISK [DoDI 3216.02, section 3, para 3.8b]

The definition of minimal risk based on the phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests" shall not be interpreted to include the inherent occupational risks certain categories of human subjects face in their everyday life, such as those encountered by service members, law enforcement, or first responders while on duty, those resulting from or associated with high-risk behaviors or pursuits, or those experienced by individuals whose medical conditions involved frequent tests or constant pain

DoD-AFFILIATED PERSONNEL AS SUBJECTS AND UNDUE INFLUENCE [DoDI 3216.02, section 3, para 3.9f]

If the human subjects research involves DoD-affiliated personnel as subjects and includes any risks to their fitness for duty (e.g. health, availability to perform job, data breach), the informed consent document must inform the personnel about these risks and that they should seek command or DOD Component guidance before participating. The consent document must also include, if applicable, potential risks for the revocation of clearance, credentials, or other privileged access or duty. Principal Investigators must receive command or DOD component approval to do any research with DoD-affiliated personnel.

Supervisors (e.g., military and civilian supervisors, officers, and others in the chain of command) are prohibited from influencing their subordinates to participate in human subjects research. Supervisors must not be present at any human subject recruitment sessions or during the consent process. Excluded supervisors or those in the chain of command may participate in separate recruitment sessions. Service members and all Reserve Component and National Guard members in a federal duty status are considered to be adults. If they are under 18 years of age, the IRB must carefully consider the recruitment process and the necessity of including such member as a human subject.

For research involving service members as human subjects that has been determined to be greater than minimal risk and when recruitment occurs in a group setting, the IRB shall appoint an ombudsperson who is not part of the research team and does not have a conflict of interest with the research. The ombudsperson shall be present during the recruitment in order to monitor that the recruitment and

informed consent explain that participation is voluntary and that the information provided about the research is consistent with the IRB-approved script and materials, including digitally provided materials. The ombudsperson should be available to address any concerns about participation. Compensation to DoD-affiliated personnel for participation in research while on duty is prohibited by federal law.

RESEARCH INVOLVING LARGE SCALE GENOMIC DATA COLLECTED ON DOD-AFFILIATED PERSONNEL [DoDI 3216.02, section 3.10]

DoD-supported research involving large scale genomic data (LSGD) collected on DoD-affiliated personnel is subject to additional requirements. Disclosure of this data may pose a risk to national security; accordingly, such research requires administrative, technical, and physical safeguards commensurate with risk, including the secondary use or sharing of de-identified data or specimens. All research involving LGSD collected from DoD-affiliated personnel will apply an HHS Certificate of Confidentiality and is subject to DoD Component security review to ensure the adequacy of the proposed administrative, technical and physical safeguards, including the secondary use or sharing of de-identified data or specimens.

ADDITIONAL PROTECTIONS FOR PREGNANT WOMEN, PRISONERS, AND CHILDREN (Subparts B, C and D of 45 CFR 46) – [DoDI 3216.02, section 3 para 3.9b, c, and d]

DoD-Supported Research involving pregnant women, prisoners, and children and other subjects who are likely to be vulnerable to coercion or undue influence are subject to additional protections set forth in the DHHS Common Rule at 45 CFR 46, Subparts B, C and D. The following additional safeguards must be provided in DoD-Supported Research: DoD-Supported Research involving pregnant women, prisoners, and children and other subjects who are likely to be vulnerable to coercion or undue influence are subject to additional protections set forth in the DHHS Common Rule at 45 CFR 46, Subparts B, C and D. The following additional safeguards must be provided in DoD-Supported Research:

- Pregnant Women, Fetuses and Neonates as Subjects in DoD-Supported Research
    - For purposes of applying 45 CFR 46 Subpart B to DoD-Supported Research, the phrase "biomedical knowledge" shall be replaced with "generalizable knowledge."
    - The applicability of Subpart B is limited to research involving pregnant women as subjects in research that is more than Minimal Risk and includes interventions or invasive procedures to the woman or the fetus, or involving fetuses or neonates as subjects.
    - Fetal research must comply with the 42 USC sections 289g-289g-2.
- Children as Subjects in DoD-Supported Research
    - Research involving children as human subjects must comply with 45 CFR Part 46, Subpart D.
- Treatment of Detainees or Prisoners of War
    - Research involving a detainee or a prisoner of war as a human subject is prohibited, except for research activities covered by an IND or IDE when it is for the purpose of diagnosis or treatment of a medical condition in a patient.
- Prisoners as Subjects in DoD-Supported Research
    - When the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum.
    - In addition to allowable categories of research on prisoners in 45 CFR Part 46 Subpart C, two additional categories are permissible:
        - Epidemiological research that meets the waiver criteria enumerated in the Federal Register, and
        - Human subjects research that would otherwise meet exemption criteria, so long as they are approved by the IRB.

- When the IRB reviews research involving prisoners, at least one prisoner representative must be present for quorum.
- When a previously-enrolled human subject becomes a prisoner and the relevant protocol was not approved by IRB in accordance with these additional protections, the Principal Investigator shall promptly notify the IRB, which must notify the relevant HRPO and other federal agencies, as required.

UNIQUE DOD LIMITATION ON WAIVERS OF INFORMED CONSENT [DoDI 3216.02, section 3, paras 3.11 and 3.13]

In accordance with 10 USC section 980, "research involving a human being as an experimental subject" is an activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction.

This activity does not include activities that are not considered research involving human subjects, Exempt categories of research, and research involving the collection or study of existing data, documents, records, or specimens from living individuals.

For research involving a human being as an "experimental subject," informed consent must be obtained in advance from the experiment subject or the subject's legal representative if the subject cannot consent; if consent is obtained from the legal representative, the research must intend to benefit the individual subject, which shall be determined by the IRB.

The IRB may not waive these requirements, unless the requirement for informed consent is waived by the Under Secretary of Defense for Research and Engineering or such person's delegate when all of the following are met:

- The research is to advance the development of a medical product necessary to the Department of Defense;
- The research may directly benefit the individual experimental subject; and
- The research is conducted in compliance with all other applicable laws and regulations.

If the research does not involve a human being as an experimental subject, the IRB may waive the consent process in accordance with its Policies and Procedures.

For classified research, waivers of consent are prohibited.

LIMITATIONS ON COMPENSATION FOR U.S. MILITARY PERSONNEL [DoDI 3216.02, section 3, para 3.9(f)(7); Dual Compensation Act and 24 U.S.C. 30]

The Dual Compensation Act prohibits a federal employee from receiving pay from more than one position for more than an aggregate of forty (40) hours of work in one calendar week. This prohibition applies to employees paid from either appropriated or non-appropriated funds, or a combination thereof, and includes temporary, part-time and intermittent appointments. This law is not applicable to enlisted off- duty military personnel in relation to their military duty.

When research involves U.S. military personnel, limitations on dual compensation include:

- Federal personnel (civil servants or service members) participating as human subjects in DoD-Supported Research while on duty and non-federal personnel may be compensated for blood draws for research up to fifty U.S. dollars ($50) for each blood draw.
- Federal personnel are prohibited from receiving pay or compensation for general research participation during duty hours, even if the research is not federally funded or conducted.
- Non-federal personnel participating as human subjects in DoD-Supported Research may be compensated for research participation other than blood draws in a reasonable amount, as approved by the IRB according to local prevailing rates and the nature of the research. Federal personnel may be compensated for general research participation only if the federal personnel is

involved in the research when not on duty in the same way as human subjects who are not federal personnel (i.e., compensated for participating in a reasonable amount as approved by the IRB according to prevailing rates and the nature of the research). However, payment to off-duty federal personnel for general research participation may not come directly from a federal source.

REQUIREMENT FOR REPORTING [DoDI 3216.02, section 3, para 3.6b(6)(d)]

NYU Langone Health shall promptly (no longer than within 30 days) notify the relevant DoD Human Research Protection official (HRPO) and appropriate sponsor(s) of the following:

- IRB changes to human subjects research that involve changes to key investigators or institutions, decreased benefit or increased risk to subjects in greater than minimal risk research, addition of vulnerable populations, or DoD-affiliated personnel as subjects;
- Transfer of human subjects research oversight to a different IRB;
- Notification by any federal body, State agency, official governing body of a Native American or Alaskan native tribe, other entity, or foreign government that the institution's DoD-Supported Research is under investigation;
- Any problems involving risks to subjects or others, suspension or termination of IRB approval, or any serious or continuing noncompliance pertaining to DoD-Supported Research involving human subjects;
- The results of the IRB's continuing review, if required;
- Change in status when a previously enrolled human subject becomes pregnant, or when the researcher learns that a previously enrolled human subject is pregnant, and the protocol was not reviewed and approved by the IRB in accordance with 45 CFR 46 Subpart B;
- Change in status when a previously enrolled human subject becomes a prisoner, and the protocol was not reviewed and approved by the IRB in accordance with 45 CFR 46 Subpart B; and
- A DoD-supported study's closure.

RECORDKEEPING REQUIREMENT [DoDI 3216.02, section 3, para 3.15]

Recordkeeping requirements for DoD-Supported Research with human subjects may be longer than the Common Rule's requirement. The DoD may require that records be submitted to the DoD for archiving.

Records maintained that document compliance or non-compliance with DoD requirements shall be made accessible for inspection and copying by representatives of the DoD at reasonable times and in a reasonable manner as determined by the supporting DoD Component.

CLASSIFIED RESEARCH [DoDI 3216.02, section 3, para 3.13]

Research involving human subjects is considered classified when classified information is required for IRB approval and oversight of the research; provided to human subjects or their guardians during the recruitment or consent processes in order to achieve fully effective legal consent; or provided to or by the human subjects during the course of the research. Under Secretary of Defense, Research and Engineering approval is required for all classified non-exempt DoD-Supported Research involving human subjects.

Waivers of informed consent are prohibited for this type of research.

Disclosure or use of classified information must comply with all applicable law.

ADDITIONAL REQUIREMENTS FOR DOD SPONSORED RESEARCH

- For non-Exempt research involving human subjects, the IRB must consider the scientific merit of the research. The IRB may rely on outside experts to provide an evaluation of scientific merit. [DoDI 3216.02, enclosure 3, para 4b2.]
- When conducting research in a foreign country, the IRB shall consider the cultural sensitivities in the setting where the research will take place and shall require that the Principal Investigator has

all necessary approvals and permissions to conduct research in that country in accordance with applicable law. [DoDI 3216.02, enclosure 3, para 4c2e.]
- Disclosure regarding the provisions for research-related injury follow the requirements of the DoD Component. [DoDI 3216.02, enclosure 3, para 10.]
- Surveys performed on DoD personnel must be submitted, reviewed, and approved by the DoD after the research protocol is reviewed and approved by the IRB.
- When conducting multi-site research, a formal agreement between the participating organizations is required to specify the roles and responsibilities of each party.
- For non-Exempt research involving human subjects, the IRB must consider the scientific merit of the research. [DoDI 3216.02, section 3, para 3.6.b(6)(a)1.]
- Disclosure regarding the provisions for research-related injury must include a statement that subjects may be eligible for health care services for research-related injuries at a military treatment facility and must document how institutions will care for subjects with such injuries. [DoDI 3216.02, section 3, para 3.12(b).]
- Surveys intended to be performed on DoD personnel may require approval by the DoD after the research protocol is reviewed and approved by the IRB.
- When conducting multi-site research, a formal agreement between the participating organizations is required to specify the roles and responsibilities of each party.

RESPONSIBILITIES

The Principal Investigator must ensure compliance with all additional DoD requirements for human subject protection, including any necessary approvals from DoD following IRB approval prior to starting the research. It also is the responsibility of the IRB to ensure that all additional requirements by DoD Components for human subject protection have been met before IRB approval of the research project.

10. INFORMED CONSENT

Prior to any study participation, informed consent must be sought from each prospective subject or the subject's Legally Authorized Representative, in accordance with 45 CFR §46.116.
In addition, the informed consent discussion must be appropriately documented, in accordance with 45 CFR §46.117. The IRB must approve both the informed consent process and documentation of informed consent.

10.1 INFORMED CONSENT PROCESS

No investigator may involve a human subject in research without obtaining the legally effective informed consent of the subject or the subject's Legally Authorized Representative unless a waiver of consent has been approved by the IRB in accordance with Section 10.6: Waiver or Alteration of Informed Consent in this Policy. In general, the IRB considers individuals who are unable to consent for their own clinical care to be unable to consent for research participation. Tools or instruments such as the Mini Mental Exam can also be used to determine capability to consent.

Consent must always be sought under circumstances that:

- provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate; and
- minimize the possibility of coercion or undue influence.

The IRB will consider where the consent process will take place and the individual who will be obtaining consent (e.g. the Principal Investigator, collaborator, or qualified designee) in its determination regarding the appropriateness of the consent process. When the potential subject's understanding of the research may be impaired due to the timing, location, or individuals participating in the proposed consent process, the IRB will require an alternative process.

The information that is given to the subject or the representative must be in language understandable to the subject or the representative.

The following applies to all studies submitted and approved by NYU Langone Health IRBs (including those that are duly authorized by NYU Langone Health to review NYU Langone Health studies):

- No informed consent, whether oral or written, may include exculpatory language through which the subject or the Legally Authorized Representative is made to waive or appear to waive any of the subject's legal rights.
- A person knowledgeable about the consenting process and the research to be conducted (i.e.: a member of the project's research team) must obtain the informed consent, and must be able to answer questions about the study.
- If someone other than the Principal Investigator conducts the interview and obtains consent, the Principal Investigator needs to formally delegate this responsibility and the person so delegated must have received appropriate training to perform this activity.

The following additional requirements apply to new studies submitted and approved by NYU Langone Health IRBs (including those duly authorized by NYU Langone Health) after January 21, 2019 [45 CFR 46.116(a)(5)]:

- The prospective subject or the Legally Authorized Representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.
- Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or Legally Authorized Representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.
- Informed consent in general must present information relating to the research in sufficient detail, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or Legally Authorized Representative's understanding of the reasons why one might or might not want to participate.

10.2 DEFINITIONS

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 procedures involved in the research.

See Legally Authorized Representatives.

LEGAL GUARDIAN means a person appointed by a court of appropriate jurisdiction.

10.3 BASIC REQUIREMENTS

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

The informed consent process involves three key features:

- disclosing to the prospective human subject information needed to make an informed decision in addition to following the requirements pertaining to consent covered by ICH-GCP (see "ICH-GCP Guidance");
- facilitating the understanding of what has been disclosed; and
- promoting the voluntariness of the decision about whether or not to participate in the research.

Informed consent is more than just a signature on a form. It is a process of information exchange to include reading and signing the informed consent document. The informed consent process is the critical communication link between the prospective human subject and an investigator, beginning with the initial approach of an investigator and continuing through the completion of the research study.

Investigators must have received the appropriate training and be knowledgeable about the study protocol in order that they may answer questions to help provide understanding to the study subject or potential study potential study subject.

The exchange of information between the investigator and study subject can occur via one or more of the following modes of communication, among others: face to face contact, mail, telephone; or fax.

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

These informed consent requirements are not intended to preempt any applicable federal, state, or local laws (including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe) that require additional information to be disclosed for informed consent to be legallyeffective, or any additional safeguards required by the institution for certain categories of individuals.

10.4 BASIC ELEMENTS OF INFORMED CONSENT

Informed consent must be sought from each potential subject or the subject's Legally Authorized Representative, in accordance with, and to the extent required by [45 CFR 46.116] and [21 CFR 50.25].

The basic elements of informed consent are:

- a statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental; a description of any reasonably foreseeable risks or discomforts to the subject;
- a description of any benefits to the subject or to others which may reasonably be expected from the research;
- a statement describing the extent, if any, to which confidentiality of records identifying the subject must be maintained;
- for research involving more than Minimal Risk, an explanation as to the availability of medical treatment in the case of research-related injury, including who will pay for the treatment and whether other financial compensation is available;
- 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;
- 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;
- for FDA-regulated studies, the possibility that the FDA may inspect the records needs to be included in the statement regarding subject confidentiality;
- an explanation of whom to contact to voice concerns or complaints about the research; and

- contact information for the IRB to obtain answers to questions about the research; to voice concerns or complaints about the research; to obtain answers to questions about their rights as a research subject; in the event the research staff could not be reached; and in the event the subject wishes to talk to someone other than the research staff.

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

- a statement that the particular treatment or procedure may involve risks to the subject, which are currently unforeseeable. (For example: Include when the research involves investigational test articles or other procedures in which the risks to subjects is not well known.);
- a statement that if the subject is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus, which are currently unforeseeable. (For example: Include when the research involves pregnant women or women of childbearing potential and the risk to fetuses of the drugs, devices, or other procedures involved in the research is not well known.);
- anticipated circumstances under which the subject's participation may be terminated by the Principal Investigator without regard to the subject's consent. (For example: Include when there are anticipated circumstances under which the Principal Investigator may terminate participation of a subject.);
- any additional costs to the subject that may result from participation in the research. (For example: Include when it is anticipated that subjects may have additional costs.);
- the consequences of a subject's decision to withdraw from the research. (For example: Include when withdrawal from the research is associated with adverse consequences.);
- procedures for orderly termination of participation by the subject. (For example: Include when the protocol describes such procedures.);
- a statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject. (For example: Include when the research is long term and interim information is likely to be developed during the conduct of the research.);
- the approximate number of subjects involved in the study. (For example: Include when the research involves more than minimal risk.);
- **for studies submitted and approved by NYU Langone Health IRBs (including those duly authorized by NYU Langone Health) on or after January 21, 2019 [45 CFR 46.116(b)(9)]: one of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:**
    - a statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the Legally Authorized Representative, if this might be a possibility; or
    - a statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies;
- **for studies submitted and approved by NYU Langone Health IRBs (including those duly authorized by NYU Langone Health) on or after January 21, 2019 [45 CFR 46.116(c),** a statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;
- **for studies submitted and approved by NYU Langone Health IRBs (including those duly authorized by NYU Langone Health) on or after January 21, 2019 [45 CFR 46.116(c)],** a statement regarding whether clinically relevant results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and
- **for studies submitted and approved by NYU Langone Health IRBs (including those duly authorized by NYU Langone Health) on or after January 21, 2019 [45 CFR 46.116(c),** for research involving biospecimens, whether the research will (if known) or might include

whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

Additional elements of informed consent to be applied when the research is subject to ICH-GCP (E6) are:

- a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject in addition to inclusion of any benefits or risks associated with alternatives; and
- a statement indicating that the monitor, the auditor, the IRBs, and the regulatory authority will be granted direct access to the subject's original medical records for verification of clinical trial procedures or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written consent form, the subject or the subject's Legally Acceptable Representative is authorizing such access. [ICH-GCP]

The NYU Langone Health IRBs are not implementing broad consent (allowable under the 2018 Common Rule) at this time.

10.5 SUBJECT WITHDRAWAL OR TERMINATIONS

For a variety of reasons, a subject enrolled in a research study may decide to withdraw from the research, or an investigator may decide to terminate a subject's participation in research regardless of whether the subject wishes to continue participating. Principal Investigators must plan for the possibility that subjects will withdraw from research and include a discussion, in the research protocol/research plan and consent document, of what withdrawal will mean and how it will be handled.

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

- For FDA-regulated clinical trials, when a subject withdraws from a study, the data collected on the subject to the point of withdrawal remain part of the study database and may not be removed. The consent document cannot give the subject the option of having data removed.

- For research not subject to FDA regulations, the Principal Investigator should inform subjects whether the Principal Investigator intends to either: (1) retain and analyze already collected data relating to the subject up to the time of subject withdrawal; or (2) honor a research subject's request that the Principal Investigator destroy the subject's data or that the Principal Investigator exclude the subject's data from any analysis.

When a subject's withdrawal request is limited to discontinuation of the primary interventional component of a research study, research activities involving other types of participation for which the subject previously gave consent may continue. Investigators should ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and procedures and continued follow-up in person, by phone, or via records review, of data and address the maintenance of privacy and confidentiality of the subject's information.

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

If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up, the investigator must not access or gather private information about the subject for purposes related to the study. However, an investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.

10.6 INSTITUTIONAL POLICY ON MANAGING DISRUPTIVE RESEARCH SUBJECTS

DEFINITIONS

RESEARCH TEAM MEMBER for purposes of this Policy, means the Principal Investigator and other individuals who contribute to the scientific development or execution of human subject research in a substantive, measurable way, whether or not they receive salaries or compensation. The Research Team consists of individuals who interact directly with human subjects for research activities including the consent process, analysis, and reporting of research data, and research data entry. Research Team Members include employees, faculty, medical staff, residents, fellows, students, volunteers, trainees, contractors, consultants, and agents of NYU Langone Health who are engaged in such research activities at NYU Langone Health.

UNACCEPTABLE BEHAVIOR for purposes of this Policy, means words or actions that show disrespect for the dignity of others and unreasonably interfere with conduct of research. Examples of Unacceptable Behavior include but are not limited to:

- harassment, intimidation, or discrimination of any form including but not limited to sexual harassment and discrimination or harassment based on race, religion, color, national origin, language, age, gender, gender identity or expression, ability status, or sexual orientation;
- sexual attention, advances, or inappropriate sexual language;
- treating the research environment with disrespect;
- threatening or hostile comments or conduct;
- sharing private information regarding other research subjects;
- inappropriate touching, physical aggression, or verbal and/or physical violence.

POLICY BACKGROUND AND PURPOSE

NYU Langone Health is committed to providing a safe, welcoming, and respectful research environment for all members of the NYU Langone Health community, including research subjects and researchers. Although interactions with research subjects are usually positive, there may be instances in which research staff members experience unacceptable behavior by subjects, such as verbal abuse, harassment, and/or physical aggression. Such behaviors directed towards research staff or in research areas are harmful because they have a negative effect on an individual's feelings of safety in the environment, decrease research team morale, and are a detriment to safe and effective conduct of research.

The purpose of this Policy is to outline NYU Langone Health's policies in addressing situations when a member of a research team conducting human subject research or another research subject is subjected to unacceptable behavior by a research subject.

This Policy applies to all human subject research conducted at or under the auspices of NYU Langone Health. Research subjects who engage in disruptive behavior in a clinical setting will be managed under the *Policy on*

Staff Mistreatment of Patients and *Policy on Managing Disruptive Patients and Family Members/Partners in Care*, as appropriate.

POLICY: GENERAL

Unacceptable Behavior by any research subject toward a Research Team Member or another research subject will not be tolerated or accepted. When a Research Team Member reports such behavior by a research subject, appropriate action, as outlined below, will be taken immediately to address the matter.

All research subjects and individuals consenting on behalf of the subject must be provided with a Statement on the Conduct of Participants in Research Studies document at the time of initial consent.

REPORTING UNACCEPTABLE BEHAVIOR AND POSSIBLE ACTIONS

A Research Team Member who is subjected to Unacceptable Behavior should contact the principal investigator or their designee when these situations occur to discuss the events and devise an appropriate response.

Any or all of the following actions, as appropriate, may be taken by the principal investigator or at the principal investigator's direction prior to withdrawing the subject from the study:

1. Attempt to verbally intervene/de-escalate the situation
2. Contact Patient Relations to assist in de-escalation
3. Contact Security to de-escalate or escort the subject off NYU Langone premises
4. Advance verbal or written warning to the subject of potential withdrawal from the study if behavior continues, with or without a probationary period

If, in the principal investigator's judgment and discretion, the research subject's behavior is in violation of the Statement on the Conduct of Participants in Research Studies, the principal investigator may withdraw the research subject from the study at any time, by written notice to the research subject. If the principal investigator is contemplating removal of a subject, they must consider the subject's safety in doing so.

REPORTING TO IRB

If any of the above actions is taken, the principal investigator should consider whether a report to the IRB as reportable new information ("RNI") is necessary (see Section 8.8, Reportable New Information).

REPORTING TO NYU LANGONE HEALTH DEPARTMENT OF EMPLOYEE & LABOR RELATIONS

All incidents of discrimination, harassment, and/or retaliation by a research subject against a Research Team Member must be reported to NYU Langone Health's department of Employee & Labor Relations in accordance with Human Resources Policies and Procedures, Chapter 4, Sections 4.5, *Avoiding Workplace Harassment and Discrimination*, and 4.5a, *Sexual Misconduct, Relationship Violence, and Stalking Policy*. Individuals with supervisory authority (including principal investigators) who are made aware of discriminatory, harassing or retaliatory behavior have an obligation to contact Employee & Labor Relations.

TRAINING OF RESEARCH TEAM MEMBERS

The principal investigator is responsible for ensuring that Research Team Members receive training regarding the management of Unacceptable Behavior by research subjects, and for communicating a management, reporting, and escalation plan to Research Team Members in case of Unacceptable Behavior by research subjects.

IRB SUBMISSION

For studies that may pose a greater risk of such incidents, it is recommended that Principal Investigators have a plan in place for protection of Research Team Members' safety and how Unacceptable Behavior will be managed. The plan should include a training plan for Research Team Members. Examples of types of studies, include but are not limited to, studies where research is conducted off NYU Langone Health premises or otherwise in locations not controlled by NYU Langone Health (such as nightclubs).

QUESTIONS

Any questions relating to this Policy should be directed to the Senior Director of Human Research Protections, E-mail: # IRB-INFO@nyulangone.org.

RELATED POLICIES

NYU Langone Hospitals policy, *Policy on Staff Mistreatment by Patients*

NYU Langone Hospitals policy, *Managing Disruptive Patients and Family Members/Partners in Care*

NYU Langone Health policy, *Avoiding Workplace Harassment and Discrimination*

NYU Langone Health policy, *Sexual Misconduct, Relationship Violence, and Stalking Policy*

10.7 WAIVER OF ALTERATION OF INFORMED CONSENT

The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement for informed consent, provided the IRB finds and documents that all the following conditions are met [45 CFR 46.116(f)]:

- the research involves no more than minimal risk to the subjects;
- the waiver or alteration will not adversely affect the rights and welfare of the subjects;
- the research could not practicably be carried out without the waiver or alteration;
- whenever appropriate, the subjects must be provided with additional pertinent information after participation;
- **for new research submitted and approved by NYU Langone Health IRBs (including those duly authorized by NYU Langone Health) after January 19, 2019:** if the research involves using identifiable private information or identifiable biospecimens, the IRB must additionally find that the research could not be practicably carried out without using such information or biospecimens in an identifiable format

OR

- if the research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
    - public benefit or service programs;
    - procedures for obtaining benefits or services under those programs;
    - possible changes in or alternatives to those programs or procedures; or
    - possible changes in methods or levels of payment for benefits or services under those programs; and
- the research could not practicably be carried out without the waiver or alteration [45 CFR 46.116(e)]. For such research, the IRB may waive the requirement to obtain informed consent if the IRB satisfies the conditions set forth above for waiver or alteration generally.

In addition, the following applies to new research submitted and approved by NYU Langone Health IRBs (including those duly authorized by NYU Langone Health) after January 19, 2019 [45 CFR 46.116(g):

The IRB may approve a research protocol in which information or biospecimens will be obtained for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without requiring the informed consent of the prospective subject or their Legally Authorized Representative or a waiver of consent, if, through the protocol: (1) the Principal Investigator will obtain information through oral or written communication with the prospective subject or Legally Authorized Representative; or (2) the Principal Investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens. The IRB must find and document that the protocol reflects that the information will be obtained in these ways and review a form to be completed by the Principal Investigator.

Note: Informed consent cannot be waived under these criteria for FDA-regulated research. Note that some research involving FDA-regulated products is not FDA-regulated and that some research that does not involve FDA-related products is FDA-regulated. Exceptions from the FDA requirements for informed consent may be waived for emergency situations [21 CFR 50.23] or for emergency research [21 CFR 50.24].

10.8 DOCUMENTATION OF INFORMED CONSENT (SIGNED CONSENT)

Informed consent must be appropriately documented, in accordance with, and to the extent required by [45 CFR 46.117] or [21 CFR 50.27]. Informed consent is documented by the use of a written informed consent form approved by the IRB and signed and dated by the subject or the subject's Legally Authorized Representative at the time of consent. A copy of the signed and dated informed consent form must be given to

the person signing the informed consent form; that is, either the subject or his/her Legally Authorized Representative).

The consent form may be either of the following approved by the IRB:

[pre-2018 Common Rule]:

- A written consent document that embodies the elements of informed consent may be read to the subject or the subject's Legally Authorized Representative, but the subject or representative must be given adequate opportunity to read it before it is signed; or

- A short form written consent document stating that the elements of informed consent have been presented orally to the subject or the subject's Legally Authorized Representative. When this method is used:
    - a witness to the oral presentation is required; and
    - the IRB must approve a written summary of what is to reviewed with the subject or representative. The long form English IRB-approved consent document may be used as the required written summary; and
    - the witness must sign both the short form attesting to the adequacy of the consent process and a copy of the summary. The subject may only sign the short form; and
    - for subjects who do not speak English, the witness must be conversant in both English and the language of the subject.
    - the person actually obtaining consent must sign a copy of the summary; and
    - a copy of the summary must be given to the subject or representative, in addition to a copy of the short form.

[2018 Common Rule]:

- A written informed consent form that meets the requirements of informed consent. The subject or the subject's Legally Authorized Representative must be given adequate opportunity to read the informed consent form before it is signed. Alternatively, this form may be read to the subject or the subject's Legally Authorized Representative; or

- A short form written informed consent form stating that the elements of informed consent have been presented orally to the subject or the subject's Legally Authorized Representative and that key information required by 45 CFR 46.116(a)(5)(i) was presented first to the subject before any other information (if any) was provided. When the short form written consent method is used:
    - a witness to the oral presentation is required; and
    - the IRB must approve a written summary of what is reviewed with the subject or Legally Authorized Representative. The long form English IRB-approved consent document may be used as the required written summary; and
    - the witness must sign both the short form and a copy of the summary. The witness is attesting to the adequacy of the consent process The subject may only sign the short form;
    - for subjects who do not speak English, the witness must be conversant in both English and the language of the subject.
    - the person actually obtaining consent must sign a copy of the summary; and
    - a copy of the summary must be given to the subject or Legally Authorized Representative, in addition to a copy of the short form.

More guidance on the documentation of and consenting process for non-English speaking subjects may be found in this Policy, Section 10.12, Consent and Language Barriers.

10.9 WAIVER OF DOCUMENTATION OF INFORMED CONSENT (WAIVER OF SIGNED CONSENT)

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

- The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality, and the research is not FDA-regulated, or

  Note: Subjects must be asked whether they want documentation linking them with the research, and their wishes must govern. Example: domestic violence research where the principal risk is discovery by the abuser that the subject is talking to researchers.

- The research presents no more than Minimal Risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. Procedures such as non-sensitive surveys, questionnaires and interviews generally do not require written consent when conducted by non-researchers; or

- **For new studies submitted and approved by NYU Langone Health IRBs (including those duly authorized by NYU Langone Health) after January 21, 2019 only**: If the subjects or Legally Authorized Representatives are members of a distinct cultural group or community in which signing forms is not the norm, the research presents no more than Minimal Risk of harm to subjects, and there is an appropriate alternative mechanism for documenting that informed consent was obtained.

In cases in which the IRB grants a waiver of the requirement for signed consent, the Principal Investigator must provide in the application materials a written summary of the information to be communicated to the subject, and the IRB will consider whether to require the Principal Investigator to provide subjects or Legally Authorized Representatives with a written statement regarding the research.

10.10 REVIEW AND APPROVAL OF THE INFORMED CONSENT FORM

The IRB is responsible for the review and approval of the informed consent form prepared by the Principal Investigator. The wording on the informed consent form must contain all of the required elements and meet all other requirements as described in this Section. If the wording of the informed consent has been initially prepared by an external entity (e.g., a pharmaceutical company or a cooperative study group, including National Cancer Institute (NCI) groups) other than by the Principal Investigator, the Principal Investigator must prepare the consent using the institutional IRB consent template.

IRB approval of the consent form language must be documented through the use of a certification stamp on each page that indicates the date of the most recent IRB approval of the document and the expiration date. If the consent form is amended during the protocol approval period, the form must bear the approval date of the amendment rather than the date of the approved protocol.

10.11 PARENTAL PERMISSION AND ASSENT

For policies on parental permission and assent in research involving children, see: *Parental Permission and Assent*.

10.12 SURROGATE CONSENT

Any use of surrogate consent requires prior approval by the IRB. See *Persons who Lack Capacity to Provide Informed Consent for Research and Surrogate Consent*.

10.13 CONSENT AND LANGUAGE BARRIERS

CONSENT DOCUMENTATION

If a study subject does not clearly understand the information presented at the signing of the consent document or in subsequent discussions, his/her consent may not be informed, and therefore, not effective.

Documentation of consent for studies where non-English-speaking subjects are enrolled (either planned or unexpectedly) is required if the IRB has not granted a Waiver of Documentation of Informed Consent. In these cases, there are two methods of documenting consent: use of a short form for when a non-English-speaking subject is encountered unexpectedly, or use of a fully translated informed consent document when enrollment of non-English-speaking subjects is planned.

TRANSLATED LONG FORM

For studies where non-English-speaking subjects are anticipated or planned to be included, researchers should submit to the IRB both English language and translated consent forms. The IRB will request an explanation of the translations and evidence of the comparability of the English and non-English consent forms. The IRB may consult with language experts or require a "back-translation" into English. The translation should provide documentation to verify the accuracy of the translation and back-translation. When non-English-speaking subjects enroll, they and the witness sign the translated document. The subjects are given a copy of the signed translated consent document.

SHORT FORM

If a non-English-speaking subject is enrolled unexpectedly and there is not an existing IRB-approved long form informed consent document available in the prospective subject's language, the Principal Investigator must follow the procedures for a "short form" written consent (see: *Documentation of Informed Consent (Signed Consent)*). Researchers may rely on an oral translation of the English language consent form by an interpreter, but should take extra care in the informed consent process to ensure that the subject has understood the research and their participation. A statement in the research records (and on the English language consent form) should indicate that the oral translation took place, identify the interpreter, and document the interpreter's belief that the subject understands the study and the consent process. If the subject is a patient, a note about the oral translation should be made in the patient's research records as well. Researchers should provide a written translation of the emergency contact information for the Principal Investigator or study team member in case the subject experiences problems.

USE OF INTERPRETERS IN THE CONSENT PROCESS

NYU Langone Health strongly recommends use of a certified medical interpreter to assist in the consent discussion with non-English-speaking prospective subjects. Using a non-certified interpreter for the consent discussion may increase the risk that the quality of the informed consent discussion will later be called into question in the event of complications with the subject.

NYU Langone Health recognizes, however, that the use of a certified medical interpreter may not always be possible. In cases where the researcher is fluent in the subject's language, the researcher may conduct the informed consent process with use of either method of documentation of consent as noted in this Policy's section on *Documentation of Informed Consent (Signed Consent).*

Researchers should consider the level of complexity and level of study risk (as determined by the IRB) when deciding whether a non-certified interpreter will be used to facilitate the consent discussion. For example, a non-certified interpreter who is bilingual in both English and the subject's language may be adequate for a minimal risk study that measures subjects' movements and heart rate but involves no other intervention.

When the short form written consent method is used (i.e., there is no translated full consent document):
If the person obtaining consent is not fluent in the prospective subject's language, an interpreter will be necessary to deliver information in the IRB-approved consent form and/or script and to facilitate the consent discussion. The interpreter assisting with presentation of the information and obtaining consent should be someone who is independent of the subject (i.e., not a family member). Whenever possible, interpreters should be provided copies of the short form written consent and the IRB-approved consent form well before the consent discussion with the subject; ideally, 24 to 48 hours prior.

If the short form process is used with an interpreter, a witness is required and must be available to sign the short form consent document. The person who serves as the witness must be conversant in both English and the subject's language. The interpreter may serve as the witness. If the interpreter also serves as the witness, she/he may sign the short form consent document and script or the full translated consent form as the witness and should note "Interpreter" under the signature line. The person obtaining consent must document that the "short form" process was used in the progress notes of the subject's medical record, including the name of the interpreter.

If, however, the person obtaining consent is fluent in the subject's language, he or she may deliver the information, but a separate witness is required to observe the consent process and attest to the adequacy of the consent process (see *Documentation of Informed Consent*).

When a long form is used (i.e., translated full consent document):
If the person obtaining consent is not fluent in the prospective subject's language, an interpreter independent of the subject should be used to facilitate the discussion. The consent form should be signed by the witness to the consent process. The person who serves as the witness must be conversant in both English and the subject's language. The interpreter may serve as the witness.

If the person obtaining consent fluently speaks the prospective subject's language, and there is a translated consent form in the subject's language, the researcher may conduct the consent process and sign the required documents as both the researcher and the interpreter. A witness to the consent process will not be required.

NOTE: If the consent process is conducted remotely (see the IRB's guidance on e-consent) and the interpreter also serves as witness to the consent process, they may provide their interpreter license number as their signature on the short-form or long form consent document regardless of whether the short form or long form consent process is used.

BRAILLE CONSENT

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

ORAL CONSENT

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

For research that is no more than Minimal Risk, documentation of consent may be waived according to the criteria in Waiver of Documentation of Informed Consent (Waiver of Signed Consent).

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

Sometimes a subject understands English but does not read or write English. An impartial witness should document that the subject understands the research and the consent process and consented to participate.

10.14 PLANNED EMERGENCY RESEARCH

NYU Langone Health permits qualified investigators to engage in responsible and ethical planned emergency research on life-threatening conditions for which available treatments are unproven or unsatisfactory and where it is not possible to obtain informed consent from research subjects or their Legally Authorized Representatives, provided the research is conducted after receipt of necessary approvals, with appropriate oversight, and in accordance will all applicable laws, rules, regulations, and institutional policies. Except as provided in this Policy, NYU Langone Health will not engage in planned emergency research without prior informed consent.

This Policy does not apply to Minimal Risk research studies for which the IRB may waive the requirement for subject informed consent. This Policy also does not apply to the emergency use of an investigational drug or biologic or unapproved medical device in a single patient.

DEFINITIONS

PLANNED EMERGENCY RESEARCH means research involving human subjects who are in need of emergency medical intervention, and who cannot give informed consent because of their life-threatening medical conditions and who do not have an available Legally Authorized Representative to provide consent.

POLICY

All Planned Emergency Research conducted by, at, or under the auspices of NYU Langone Health or funded by NYU Langone Health shall be conducted in compliance with, (i) this Policy, (ii) the requirements of the IRB, (iii) all applicable federal, state, and local laws, regulations, and policies, (iv) the terms of any grant, contract, agreement, or other funding supporting the Planned Emergency Research, and (v) all other New York University and NYU Langone Health policies. No NYU Langone Health personnel, facilities, equipment, or other resources, including funding, shall be used for any Planned Emergency Research that is not conducted in accordance with the requirements of this Policy.

APPROVALS

Planned Emergency Research may be conducted by, at, or under the auspices of NYU Langone Health or funded by NYU Langone Health only when NYU Langone Health's Senior Vice President, Clinical Research Operations & Regulatory Affairs (or a designee) has confirmed that all of the following elements are present:

1. The IRB has approved the protocol for the Planned Emergency Research.

2. Either the Food and Drug Administration (FDA) or the Department of Health and Human Services (DHHS) has approved the Planned Emergency Research, each in accordance with the applicable regulatory requirements (below).

3. Either NYU Langone Health's Chief Scientific Officer or its Senior Associate Dean for Clinical Sciences (or a designee) have determined in writing that the Planned Emergency Research is of significant importance to and furthers the research mission of NYU Langone Health.

4. NYU Langone Health's Chief Medical Officer (or a designee) and the chief medical officer(s) for the NYU Langone Health hospital(s) or other facility(ies) where the Planned Emergency Research (or a designee) will occur have determined that the research is feasible and appropriate in the planned hospital(s) or other facility(ies).

5. NYU Langone Health's Senior Vice President for Strategy, Planning and Business Development (or a designee) has evaluated the potential risks of the Planned Emergency Research and confirmed that there is insurance in place to cover those risks.

6. NYU Langone Health's Chief Financial Officer (or a designee) has evaluated the financial considerations and feasibility of the Planned Emergency Research and confirmed that the Planned Emergency Research is an acceptable financial risk and feasible for NYU Langone Health.

7. The Principal Investigator for the Planned Emergency Research is employed by NYU Langone Health.

8. The Principal Investigator has signed an acknowledgement of responsibility to ensure compliance with the protocol for the Planned Emergency Research, applicable laws and regulations, the terms of any grant, contract, or cooperative agreement covering the Planned Emergency Research, and any other conditions to the performance of the Planned Emergency Research issued pursuant to this Policy.

FDA-REGULATED

A request for an exception from informed consent of research subjects may be granted by the IRB for FDA-regulated planned research in an emergency setting if the IRB, with the written concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation, finds and documents each of the following:

- Life-Threatening Situation. The human subjects are in a life-threatening situation, which means, for purposes of this Policy, diseases or conditions in which the likelihood of death is high unless the course of the disease or condition is interrupted. An individual is not considered to be in a life-threatening situation when the situation is not emergent. For example, research involving an individual who has been in a coma for a long period of time and whose condition is not rapidly deteriorating is not considered planned emergency research. In that case, the research intervention requires consent by a Legally Authorized Representative or appropriate surrogate of the subject. See *Persons who Lack Capacity to Provide Informed Consent for Research and Surrogate Consent*.

- Available Treatments Unproven or Unsatisfactory. Available treatments are unproven or unsatisfactory, and the collection of additional valid scientific evidence is necessary to determine the safety and effectiveness of particular study interventions and/or test articles.
- Informed Consent Not Feasible. Obtaining informed consent is not feasible because:
  - The subjects will not be able to give their informed consent as a result of their medical condition;
  - The practicable treatment window does not allow time to get prospective consent, and the intervention under investigation must be administered before obtaining consent from a subject's Legally Authorized Representative or appropriate surrogate, as defined in Section Legally Authorized Representative, is feasible; and
  - There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.
- Prospect of Direct Benefit. Participation in the research holds out the prospect of direct benefit to the subjects because:
  - They are in life-threatening situations that necessitate intervention;
  - Appropriate animal and/or other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
  - Risks associated with the investigation are reasonable in relation to what is known about the medical conditions of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
- Impracticable Without Waiver. The clinical investigation could not practicably be carried out without a waiver of consent.
- Defined Therapeutic Window. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence.
- Informed Consent Procedures and Documents. The informed consent procedures and informed consent documents are consistent with the requirements of 21 CFR § 50.25. These procedures and documents are to be used with subjects or their Legally Authorized Representative or appropriate surrogate in situations where use of such procedures and documents is feasible.
- Right to Object: The procedures in place provide an opportunity for a Legally Authorized Representative or family member to object to a subject's enrollment and/or continued participation in the study. [21 CFR § 50.24(a)(6) and (7)(v)]. If such Legally Authorized Representative or family member objects to the subject's continued participation, consent should be considered to have been withdrawn and the investigator must immediately notify the IRB.

DHHS-REGULATED

When planned research in an emergency setting is not subject to FDA regulations, but is subject to DHHS regulations, a request for an exception from informed consent of research subjects may be granted by the IRB, with the written concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation, finds and documents each of the following relative to the research:

- The research is not subject to regulations codified by the FDA at 21 CFR 50.

- Life-Threatening Situation. The subjects are in a life-threatening situation, meaning that diseases or conditions in which the likelihood of death is high unless the course of the disease or condition is interrupted. An individual is not considered to be in a life-threatening situation when the situation is

not emergent. For example, research involving an individual who has been in a coma for a long period of time and whose condition is not rapidly deteriorating is not considered planned emergency research. In that case, the research intervention will require consent by a Legally Authorized Representative of appropriate surrogate of the subject. available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions. See *Persons who Lack Capacity to Provide Informed Consent for Research and Surrogate Consent*.

- Informed Consent Not Feasible. Obtaining informed consent is not feasible because:
  - The subjects will not be able to give their informed consent as a result of their medical condition;
  - The practicable treatment window does not allow time to get prospective consent, and the intervention under investigation must be administered before obtaining consent from a subject's Legally Authorized Representative or appropriate surrogate is feasible; and
  - There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.

- Prospect of Direct Benefit. Participation in the research holds out the prospect of direct benefit to the subjects because:
  - They are in life-threatening situations that necessitate intervention;
  - Appropriate animal and/or other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
  - Risks associated with the investigation are reasonable in relation to what is known about the medical conditions of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

- Impracticable Without Waiver. The research could not practicably be carried out without a waiver of consent.

- Defined Therapeutic Window. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence.

- Informed Consent Procedures and Documents. The IRB has reviewed and approved consent procedures and a consent document and has found the informed consent procedures and informed consent documents are consistent with the requirements of 45 CFR § 46.116 and 46.117. These procedures and documents are to be used with subjects or their Legally Authorized Representative or appropriate surrogate in situations where use of such procedures and documents is feasible.

- Right to Object. The IRB has reviewed and found procedures in place and information to be used provide an opportunity for a Legally Authorized Representative or family member to object to a subject's enrollment and/or continued participation in the study. If such Legally Authorized Representative or family member objects to the subject's continued participation, consent should be considered to have been withdrawn and the investigator must immediately notify the IRB.

ADDITIONAL SUBJECT PROTECTIONS – FDA AND DHHS REGULATED

Additional protections for subjects will be provided, including the following:

- Consultation (including, when appropriate, consultation to be carried out by the IRB) with representatives of the community(ies) in which the clinical investigation will be conducted and from which the subjects will be drawn;
- Public disclosure to the community(ies) in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the research, of plans for the research and its risks and expected benefits;
- Public disclosure of sufficient information following completion of the protocol to apprise the community(ies) and investigators of the study, including the demographic characteristics of the research population, and its results; and
- Establishment of an independent Data and Safety Monitoring Committee to exercise oversight of the research.
- The Principal Investigator must attempt to contact a Legally Authorized Representative or appropriate surrogate within the therapeutic window defined in the proposed investigational plan and, if feasible, to ask the Legally Authorized Representative or surrogate contacted for consent, or to provide an opportunity for the Legally Authorized Representative or surrogate to object, within that window rather than proceeding without consent. The investigator will summarize efforts made to contact the Legally Authorized Representative or appropriate surrogate and make this information available to the IRB at the time of continuing review.

Informed Consent Requirement

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

In addition, if obtaining informed consent is not feasible and a Legally Authorized Representative is not reasonably available, the Principal Investigator must, if feasible, attempt to contact within the therapeutic window the subject's family member who is not a Legally Authorized Representative, and ask whether he or she objects to the subject's participation in the research [21 CFR 50.24(a)(6))]. The Principal Investigator will notify the IRB as soon as is reasonable of such objection to participation, and the IRB will follow appropriate steps. Additionally, the Principal Investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

The IRB is responsible for ensuring that the Principal Investigator has procedures in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a Legally Authorized Representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation, and other information contained in the informed consent document.

The IRB will also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a Legally Authorized Representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a Legally Authorized Representative or family member is told about the clinical investigation and the subject's condition improves, the subject must also be informed as soon as feasible. If a subject is entered into a clinical investigation without consent and the subject dies before a Legally Authorized Representative or family member can be contacted, information about the clinical investigation must be provided to the subject's Legally Authorized Representative or family member, if feasible.

Documentation

If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the above criteria or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the Principal Investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to the FDA or DHHS (as applicable) and to the sponsor's clinical investigators who are participating, or are asked to participate, in this or a substantially equivalent clinical investigation of the sponsor, and to other IRBs that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.
The IRB determinations and documentation are to be retained by the IRB for at least three (3) years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by the FDA and/or DHHS.

IND / IDE Requirements

Protocols where an exception to the informed consent requirement under this section are granted must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as including subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments.

NYU Langone Health Requirements

In addition to IRB approval, planned emergency research conducted by or at NYU Langone Health that involves the waiver of informed consent is subject to the institutional requirements set forth in NYU Langone Health's *Policy on Planned Emergency Research* (HSR Policy #6).

10.15 POSTING OF CLINICAL TRIAL CONSENT FORM

For any Clinical Trial conducted or supported by a federal department or agency that is submitted and approved by the NYU Langone Health IRBs (including those duly authorized by NYU Langone Health) on or after January 21, 2019, one copy of the IRB-approved informed consent form that was used to enroll subjects must be posted by the awardee or the federal department or agency Component conducting the trial on a publicly available federal website that will be established as a repository for such informed consent forms [45 CFR 46.116(h)]. "Clinical Trial" is defined as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

The Principal Investigator must ensure that the last IRB-approved informed consent form is posted on the federal website after the clinical trial is closed to recruitment, and no later than sixty (60) days after the last study visit by the last subject, as required by the protocol.

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

11. VULNERABLE POPULATIONS

When some or all of the subjects in a protocol are likely to be vulnerable to coercion or undue influence, the IRB should include additional safeguards to protect the rights and welfare of these subjects. Some of

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

If the IRB reviews research that involves categories of subjects vulnerable to coercion or undue influence, the review process will include one or more individuals who are knowledgeable about or experienced in working with these subject populations will be included in the review process.

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

Under each IRB's FWA (NYUGSoM, NYUGLISoM, duly authorized external IRB), the subparts apply to all research regardless of funding source.

Researchers conducting human subjects research must check with the IRB to determine applicability of and how to apply the subparts.

Subpart B

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

Subpart C

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

Subpart D

Additional Protections for Children Involved as Subjects in Research

11.1 PI RESPONSIBILITIES

The Principal Investigator is responsible for identifying the potential for enrolling vulnerable subjects in the research proposal at initial review and for providing justification for including vulnerable populations in the research. For example, the Principal Investigator is responsible for identifying patients who are at risk for impaired decisional capacity as a consequence of psychiatric illness, and who are being asked to participate in a research study with greater than Minimal Risk.

11.2 IRB RESPONSIBILITIES

- The IRB shall include representation, either as members or ad hoc consultants, individual(s) interested in or who have experience with the vulnerable populations involved in a research proposal.
- The IRB reviews the PI's justifications for including vulnerable populations in the research to assess appropriateness of the research proposal.
- The IRB must ensure that additional safeguards have been included in each study to protect the rights and welfare of vulnerable subjects as needed at the time of initial review of the research proposal.
- Information reviewed as part of the continuing review process should include the number of subjects considered as members of specific vulnerable populations.

- For studies that do not have or are not required to have a Data and Safety Monitoring Board (DSMB) or aData Monitoring Committee and have entered vulnerable subjects, the IRB needs to carefully review the safety monitoring plan.
- The IRB should be knowledgeable about and experienced in working with populations who are vulnerable to coercion and undue influence. If the IRB requires additional qualification or expertise to review a protocol, it should obtain consultation.

INITIAL REVIEW OF RESEARCH PROPOSAL

- The Principal Investigator should identify the potential to enroll vulnerable subjects in the proposed research at initial review and provide the justification for their inclusion in the study.
- The IRB will evaluate the proposed plan for consent of the specific vulnerable populations involved. If the research involves adults unable to consent, the IRB evaluates the proposed plan for permission of Legally Authorized Representatives.
- The IRB evaluates and approves the proposed plan for the assent of subjects.
- The IRB evaluates the research to determine the need for additional protections and consider the use of a DSMB or data monitoring committee as appropriate.
- The Principal Investigator should provide appropriate safeguards to protect the subject's rights and welfare, which may include the addition of an independent monitor. The independent monitor is a qualified individual not involved in the research study who will determine the subject's capacity to provide voluntary informed consent.
- Examples of studies that warrant independent monitoring include those involving schizophrenic patients who will be exposed to placebo, and/or drug washout, and/or treatment with agents that are not approved by the Food and Drug Administration (FDA). Populations requiring independent monitoring would include individuals with schizophrenia, other psychotic disorders or conditions characterized by lack of reality testing (i.e., psychosis). Populations not usually requiring independent monitoring would include those with substance use disorders.
- The IRB will assess the adequacy of additional protections for vulnerable populations provided by the Principal Investigator.

CONTINUING REVIEW AND MONITORING

At continuing review, the Principal Investigator should identify the number of vulnerable subjects enrolled and any that needed an independent monitor in the study progress report.

11.3 RESEARCH INVOLVING CHILDREN

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

DEFINITIONS

CHILD under DHHS and FDA regulations, is a person who has 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.

When research is conducted in New York State, persons who meet the above definition are all individuals under 18 years of age with the following exceptions:

Individuals between 16 and 18 years of age adjudicated as emancipated by a probate court

All individuals under 18 years of age, if the research procedures are limited to:

- HIV testing, counseling, and treatment;
- Outpatient mental health services;
- Testing or treatment for sexually transmitted diseases;
- Treatment or rehabilitation for alcohol or drug dependence; and/or
- Abortion counseling and treatment.

All individuals between 16 and 18 years of age, if the research procedures are limited to inpatient mental health services

NOTE: For research conducted in jurisdictions other than New York State, the research must comply with the laws regarding the legal age of consent in all relevant jurisdictions. The Office of General Counsel may be consulted to for assistance with regard to the laws in other jurisdictions.

GUARDIAN under DHHS and FDA regulations means an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care. When research is conducted in New York State, the persons who meet the definition of guardian are court-appointed guardians with the authority to consent to major medical, psychiatric or surgical treatment with specific authorization to consent to research.

NOTE: For research conducted in jurisdictions other than New York State, the research must comply with the laws regarding guardianship in all relevant jurisdictions. The Office of General Counsel may be consulted to assistance with regard to the laws in other jurisdictions.

ASSENT means a child's affirmative agreement to participate in research. Mere failure to object, absent affirmative agreement, should not be construed as assent.

PERMISSION means the agreement of parent(s) or legal guardian to the participation of their child or ward in research.

PARENT means a child's biological or adoptive parent.

ALLOWABLE CATEGORIES

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

1. Research that does not involve physical or emotional risk greater than that ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (i.e., minimal risk). [45 CFR 46.404]
    - Requires assent of the child.
    - Requires permission of either both parents, or legal guardian, unless one parent is deceased, unknown, incompetent, or not reasonably available; or only one parent has legal responsibility for the care and custody of the child.
    - The IRB may determine that the permission of one parent is sufficient, even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.
2. Research involving greater than Minimal Risk but presenting the prospect of direct benefit to the individual subject. [45 CFR 46.405]
    - The risk must be justified by the anticipated benefit to the subjects.
    - Requires assent of the child.
    - Requires permission of either both parents, or legal guardian, unless one parent is deceased, unknown, incompetent, or not reasonably available; or only one parent has legal responsibility for the care and custody of the child.
    - The IRB may determine that the permission of one parent is sufficient, even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

3. Research involving greater than Minimal Risk with no reasonable prospect of direct benefit to the individual subject, but is likely to yield generalizable knowledge about the subject's disorder or condition. [45 CFR 46.406]
    - The risk represents a minor increase over Minimal Risk.
    - The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations.
    - Requires permission of either both parents, or legal guardian, unless one parent is deceased, unknown, incompetent, or not reasonably available; or only one parent has legal responsibility for the care and custody of the child.
    - Requires assent of the child.
4. Research that is not otherwise approvable but which presents an opportunity to understand, prevent, or alleviate serious problems affecting the health or welfare of children. [45 CFR 46.407]
    - Federally-funded research in this category must be approved by the Secretary of Health and Human Services, and requires consent of either both parents, or legal guardian.
    - FDA-regulated research in this category must be approved by the Commissioner of Food and Drugs.
    - For non-federally-funded research and non-FDA research, IRB will consult with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law). Based on the recommendation of the panel, the IRB may approve the research based on either:
        - That the research in fact satisfies the conditions of the previous categories, as applicable; or
        - The following:
            - the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
            - the research will be conducted in accord with sound ethical principles; and
            - informed consent will be obtained in accord with the provisions for informed consent and other applicable sections of this Policy manual.

PARENTAL PERMISSION AND ASSENT

PARENTAL PERMISSION

In accordance with [45 CFR 46.408(b)] and [21 CFR 50.55(e)], the IRB must determine that adequate provisions have been made for soliciting the permission of each child's parents or guardians.

Permission from both parents is required for all research to be conducted with children unless: (1) one parent is deceased, unknown, incompetent, or not reasonably available; or (2) when only one parent has legal responsibility for the care and custody of the child; or (3) the research falls under 1 and 2 above and the IRB has determined that the permission of one parent is sufficient.

Parents or guardians must be provided with the basic elements of consent as stated in [45 CFR 46.116(a)(1-8)] and [21 CFR 50.25(a)(1-8)] and any additional elements the IRB deems necessary.

The IRB may find that the permission of one parent is sufficient for research to be conducted under [45 CFR 46.404] (21 CFR 50.51) or [45 CFR 46.405] (21 CFR 50.52). The IRB's determination of whether consent must be obtained from one or both parents will be documented in the consent checklist when a protocol receives expedited review, and in meeting minutes when reviewed by the convened IRB.

Consent from both parents is required for research to be conducted under [45 CFR 46.406] (21 CFR 50.53) and [45 CFR 46.407] (21 CFR 50.54) unless:

- one parent is deceased, unknown, incompetent, or not reasonably available; or

- when only one parent has legal responsibility for the care and custody of the child

The IRB may waive the requirement for obtaining consent from a parent or legal guardian for research that is not FDA-regulated if both of the following are true: (1) the research meets the provisions for waiver in [45 CFR 46.116(d)(1-4)]; or the IRB determines that the research protocol is designed for conditions or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), and (2) an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, 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 research subjects, as well as their age, maturity, status, and condition.

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

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

ASSENT FROM CHILDREN

Because "assent" means a child's affirmative agreement to participate in research [45 CFR 46.402(b)], where a child's assent is required, the child must actively show his or her willingness to participate in the research, rather than just complying with directions to participate and not resisting in any way. The IRB has the discretion to judge children's capacity to assent for all of the children to be involved in a proposed research activity, or on an individual basis.

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

The IRB presumes that children ages 7 and older should be given an opportunity to provide assent. Generally, oral assent through the use of a script should be obtained from children 7-11 years of age. Written assent using a written document for the children to sign may be sought for older children. If the child's assent is not obtained the Principal Investigator may either re-approach the child at a later time or not enroll the child.

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

If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research.

Even when the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances detailed in the Waiver of Informed Consent.

THE ASSENT FORM

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

The assent form should be drafted in a way that is age appropriate and study-specific, taking into account the typical child's experience and level of understanding, and the document should be composed in a way that treats the child respectfully and conveys the essential information about the study. The assent form should:

- tell why the research is being conducted;
- describe what will happen and for how long or how often;
- say it is up to the child to participate and that it is okay to say no;
- explain if it will hurt and if so for how long and how often;
- say what the child's other choices are;
- describe any good things that might happen;
- say whether there is any compensation for participating; and
- ask for questions.

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

CHILDREN WHO ARE WARDS

Children who are wards of the State or any other agency, institution, or entity can be included in research involving greater than Minimal Risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition, only if such research is:

- related to their status as wards; or
- conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

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

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

RE-CONSENT UPON REACHING AGE OF MAJORITY

If the IRB determines that a child's assent is required under the federal regulations, the IRB must also determine whether re-consent is required when the subject reaches the age of legal majority during study participation in order for research-required interactions or interventions to continue. The NYU Langone Health IRB will require re-consent when a research subject who was a minor and entered the study with parental or guardian consent reaches the age of majority (in New York State, age 18) while continuing in the research. Re-consent is also necessary if previously collected biospecimens are still being utilized or if those subjects' medical records will continue to be accessed/reviewed.

11.4 RESEARCH INVOLVING PREGNANT WOMEN, HUMAN FETUSES AND NEONATES

DEFINITIONS

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

DELIVERY refers to a complete separation of the fetus from the woman by expulsion or extraction or any other means.

FETUS means the product of conception from implantation until delivery.

NEONATE means a newborn.

NON VIABLE NEONATE means a neonate after delivery that, although living, is not viable.

PREGNANCY encompasses the period of time from implantation until delivery. A woman is assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

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

RESEARCH INVOLVING PREGNANT WOMEN OR FETUSES

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:

- Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risk to pregnant women and fetuses.
- 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.
- Any risk is the least possible for achieving the objectives of the research.
- If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, then the consent of the pregnant woman must be obtained in accord with the provisions for informed consent.
- If the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father must be obtained in accord with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
- Each individual providing consent under previous two elements of this Section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.
- For children who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent under Parental Permission and Assent.
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy.

- Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.
- Individuals engaged in the research will have no part in determining the viability of a neonate.

DHHS-funded research that falls in this category must be approved by the Secretary of Health and Human Services. If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates, and the research is not approvable under the above provisions, then the research will be sent to OHRP for DHHS review.

RESEARCH INVOLVING NEONATES

The following Policies and Procedures apply to all research involving neonates, regardless of funding source.

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 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 set forth in *Neonates of Uncertain Viability or Nonviable Neonates* (see below in this Section) have been met as applicable.

NEONATES OF UNCERTAIN VIABILITY

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

The IRB determines that:

- 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 the provisions of permission and assent, except that the consent of the father or his Legally Authorized Representative need not be obtained if the pregnancy resulted from rape or incest.

NON VIABLE NEONATES

After delivery, nonviable neonates 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.
- The legally effective informed consent of both parents of the neonate is obtained in accord with the provisions of permission and assent, except that the waiver and alteration of the provisions of permission and assent do not apply.

However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a Legally Authorized Representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

VIABLE NEONATES

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

RESEARCH INVOLVING, AFTER DELIVERY, THE PLACENTA, THE DEAD FETUS, OR FETAL MATERIAL

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

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

RESEARCH NOT OTHERWISE APPROVABLE

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:

- that the research in fact satisfies the conditions of *Research Involving Pregnant Women or Fetuses*, as applicable; or
- the following:
    - the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
    - the research will be conducted in accord with sound ethical principles, and
    - informed consent will be obtained in accord with the provisions for informed consent and other applicable sections of this Policy manual.

11.5 RESEARCH INVOLVING PRISONERS

Prisoners are another of the three classes that are deemed so vulnerable to exploitation in research that there are special rules in the federal regulations protecting them. In the past, prisoners were viewed as a convenient research population, due to their being housed in a single location, constituting a large and relatively stable population, and living a routine life. Unfortunately, all the things that make prisoners a convenient research population also make prisoners ripe for exploitation.

The concern that Subpart C, and this Policy based on Subpart C, attempt to address is whether prisoners have any real choice in participation in research, or whether incarceration could affect their ability to make a truly voluntary, uncoerced decision to participate as subjects in research, prohibiting free choice. It is the purpose of this Policy to provide additional safeguards for the protection of prisoners involved in research activities to which this Subpart is applicable. [45 CFR 46.302]

The following Policy applies to all biomedical and behavioral research involving prisoners as subjects, regardless of funding source. The requirements in this section are consistent with [Subpart C of 45 CFR 46], which applies to DHHS- funded research.

Even though the IRB may approve a research protocol involving prisoners as subjects according to this Policy, Principal Investigators are still subject to any applicable state or local laws such as, in New York State, the Administrative Regulations of the New York Department of Corrections. [45 CFR 46.301]

DEFINITIONS

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.

MINIMAL RISK means, for research involving prisoners, the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons [45 CFR 46.303(d); 21 CFR 50.3(o).This differs from the definition as stated in 45 CFR 46.102(i) and 21 CFR 50.3(k).

COMPOSITION OF THE IRB

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

- A majority of the IRB (exclusive of prisoner members) must have no association with the prison(s) involved, apart from their membership on the IRB; and
- At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one IRB, only one IRB need satisfy this requirement.

ADDITIONAL DUTIES OF THE IRB

In addition to all other responsibilities prescribed for IRB in the *Institutional Review Board* and NYU Langone Health *IRB Review Process* sections of this Policy manual (Sections 5 and 8), the IRB will review research involving prisoners and approve such research only if it finds that:

- the research falls into one of the following permitted categories [45 CFR 46.306]:
    - study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
    - study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
    - research on conditions particularly affecting prisoners as a class (for example, research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults); or
    - research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject.
- any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

- the risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;
- procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the Principal Investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;
- the information is presented in language which is understandable to the subject population;
- adequate assurance exists that a parole board will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and
- where the IRB finds there may be a need for follow-up examination or care of subjects after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing subjects of this fact.

CERTIFICATION TO HHS

Under [45 CFR 46.305(c)], the institution responsible for conducting research involving prisoners that is supported by HHS shall certify to the Secretary (through OHRP) that the IRB has made the seven findings required under [45 CFR 46.305(a)]. For all HHS conducted or supported research, the

NYU Langone Health IRB will send to OHRP a certification letter to this effect, which will also include the name and address of the institution and specifically identify the research protocol in question and any relevant HHS grant application or protocol. HHS conducted or supported research involving prisoners as subjects may not proceed until OHRP issues its approval in writing to the NYU Langone Health IRB on behalf of the Secretary under [45 CFR 46.306(a)(2)].

Under its authority at [45 CFR 46.115(b)], OHRP requires that the institution responsible for the conduct of the proposed research also submit to OHRP a copy of the research proposal so that OHRP can determine whether the proposed research involves one of the categories of research permissible under [45 CFR 46.306(a)(2)], and if so, which one.

- The term "research proposal" as used above includes the IRB-approved protocol, any relevant HHS grant application or proposal, any IRB application forms required by the IRB, and any other information requested or required by the IRB to be considered during initial IRB review.
- The above requirement does not apply to research that is not HHS conducted or supported.
- Involved in research activities to which this subpart is applicable. [45 CFR 46.302]

INCARCERATION OF ENROLLED SUBJECTS

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

1. Confirm that the subject meets the definition of a prisoner.
2. Consult with the Principal Investigator to determine if it is in the best interests of the subject to continue participation in the study, in part or in full, and if so, if there are specific study activities which are in the best interests of the subject and should continue until the IRB is able to review the research study under Subpart C.
3. If the subject should continue, one of two options are available:

    a) Keep the subject enrolled in the study and review the research under Subpart C. If some of the requirements of Subpart C cannot be met or are not applicable (e.g., procedures for the selection of subjects within the prison), but it is in the best interests of the subject to remain

in the study, keep the subject enrolled and inform OHRP of the decision along with the justification.

b) Remove the subject from the study and keep the subject on the study intervention under an alternate mechanism such as compassionate use, off label use, etc.

4. If a subject is incarcerated temporarily while enrolled in a study:
   a. If the temporary incarceration has no effect on the study (i.e., there is no need for study activities to take place during the temporary incarceration), keep the subject enrolled.
   b. If the temporary incarceration has an effect on the study, follow the above guidance.

REQUIREMENTS OF THE PRISONER REPRESENTATIVE

For research reviewed by the convened IRBs involving prisoners:

- The prisoner representative must be a voting member of the IRB.
- The prisoner representative must review research involving prisoners and must receive all materials pertaining to the research (same as primary reviewers).
- The prisoner representative must be present at a convened meeting when the research involving prisoners is reviewed. If the prisoner representative is not present, research involving prisoners cannot be reviewed or approved.
- The prisoner representative must present his/her review either orally or in writing at the convened meeting of the IRB when the research involving prisoners is reviewed.
- Minor modifications to previously approved research may be reviewed using the expedited procedure described below, using either of the two procedures described based on the type of modification.
- Substantial modifications reviewed by the convened IRBs must use the same procedures for initial review including the responsibility of the prisoner representative.
- Continuing review–must use the same procedures for initial review including the responsibility of the prisoner representative.

For research reviewed by the expedited procedure involving interaction with prisoners (including obtaining consent from prisoners):

- Research involving prisoners involving interaction with prisoners (including obtaining consent from prisoners) may be reviewed by the expedited procedure, if a determination is made that the research is Minimal Risk for the prison population being studied or included.
- The prisoner representative must concur with the determination of Minimal Risk.
- The prisoner representative must review the research as a reviewer or consultant. This may be as the sole reviewer of in addition to another reviewer or in place of another reviewer as appropriate.
- Review of modifications and continuing review must use the same procedures for initial review using this expedited process including the responsibility of the prisoner representative.

For research reviewed by the expedited procedure that does not involve interaction with prisoners (e.g. research involving existing data or record review):

- Research involving prisoners that does not involve interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research is Minimal Risk for the prison population being studied or included.
- The prisoner representative may review the research as a reviewer or consultant if designated by the IRB chair, but review by the prisoner representative is not required.
- Review of modification and continuing review must use the same procedures for initial review using this expedited process including the responsibility of the prisoner representative.

WAIVER FOR EPIDEMIOLOGY RESEARCH

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

- Studies in which the sole purposes are:
  - to describe the prevalence or incidence of a disease by identifying all cases, or
  - to study potential risk factor associations for a disease, and
  - where the IRB has approved the research and fulfilled its duties under [45 CFR 46.305(a)(2)–(7)] and determined and documented that:
    - the research presents no more than Minimal Risk and no more than inconvenience to the prisoner- subjects, and
    - prisoners are not a particular focus of the research.

The specific type of epidemiological research subject to the waiver should involve no more than Minimal Risk and no more than inconvenience to the human subjects. The waiver would allow the conduct of minimal risk research that does not now fall within the categories set out in [45 CFR 46.306(a)(2)].

The range of studies to which the waiver would apply includes epidemiological research related to chronic diseases, injuries, and environmental health. This type of research uses epidemiologic methods (such as interviews and collection of biologic specimens) that generally entail no more than Minimal Risk to the subjects.

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

11.6 PERSONS WHO LACK CAPACITY TO PROVIDE INFORMED CONSENT FOR RESEARCH AND SURROGATE CONSENT

Individuals with reduced or impaired decision-making capacity may not be able to understand or appreciate information necessary to make a voluntary and informed decision about participating in research. Such individuals may be vulnerable to coercion and undue influence. This Policy is designed to protect the rights and welfare of these individuals, while also facilitating research into the very conditions and disorders which affect them.

This Policy applies to all research involving individuals 18 years of age or older who lack or who may lack the capacity to make a voluntary and informed decision to participate in research. This Policy applies to all such research regardless of funding source. Any research involving individuals who lack or who may lack capacity also must comply with applicable law, including those relating to assessment of capacity, authority to make health care decisions on behalf of another individual, and research involving persons living in an institution.

GENERAL REQUIREMENTS FOR SURROGATE CONSENT

Obtaining research informed consent from a representative of a subject who is 18 years of age or older rather than directly from the subject ("surrogate consent") requires prior approval of the IRB. Surrogate consent may be used only for such individuals who lack capacity to provide their own consent. Surrogate consent may be provided only by the subject's Legally Authorized Representative (as defined in Section *Legally Authorized Representatives*).

APPROVAL CRITERIA FOR RESEARCH INVOLVING USE OF SURROGATE CONSENT

The IRB may approve use of surrogate consent only for studies that have the prospect of direct benefit to subjects directly or will answer a scientific question that will further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of the studied population, thereby benefitting those similarly situated in the future. Within this framework, the IRB may approve use of surrogate consent for research only if the research belongs to one of the following categories.

1. Research involving interventions or procedures that are considered minimal risk and present the prospect of direct benefit to the individual subject. The IRB may approve such studies if the risks are reasonable in relation to the prospective benefits. For new protocols, this is the only category of research involving surrogate consent that may be eligible for expedited review, subject to all other requirements as described in *IRB Policies and Procedures,* Expedited Review of Research.
2. Research involving interventions or procedures that are considered minimal risk and have no prospect of direct benefit to the individual subject, but are likely to yield generalizable knowledge about the subject's disorder or condition. The IRB may approve such studies if important to advance to the scientific knowledge of a medical condition that affects the research population, and if the risks are reasonable in relation to such importance. For research in this category, the disorder, condition or factor that prevents the individual from having capacity to consent must be an intrinsic characteristic of the research population such that the research could not otherwise be conducted on subjects who have capacity.
3. Research involving interventions or procedures that are considered a minor increase over minimal risk but present the prospect of direct benefit to the individual subject. The IRB may approve such studies only if the risks are reasonable in relation to the prospective benefits, if the potential benefits are similar to those available in the standard clinical or treatment setting, and if the risk-benefit ratio is favorable to subjects.
4. Research involving interventions or procedures that are considered a minor increase over minimal risk and have no prospect of direct benefit to the individual subject, but are likely to yield generalizable knowledge about the subject's disorder or condition. The IRB may approve such studies if vitally important to advance to the scientific knowledge of a medical condition that affects the research population, and if the risks are reasonable in relation to such vital importance. For research in this category, the disorder, condition or factor that prevents the individual from having capacity to consent must be an intrinsic characteristic of the research population such that the research could not otherwise be conducted on subjects who have capacity.
5. Research involving interventions or procedures that are considered a more than a minor increase over minimal risk but present the prospect of direct benefit to the individual subject. The IRB may approve such studies only if the risks are reasonable in relation to the prospective benefits, if the potential benefits are similar to those available in the standard clinical or treatment setting, and if the risk-benefit ratio is favorable to subjects. Such ratios are less favorable when the risk is substantially more than a minor increase over minimal risk. Such ratios are more favorable when the prospect of direct benefit is more certain, or the benefit is expected to be more frequent or more significant.

In order to determine whether an intervention or procedure is a "minor increase over minimal risk" or if research is "vitally important," the IRB will apply, as appropriate, principles for reviewing research involving children under federal regulations and applicable IRB policies.

A "minor increase over minimal risk" means that the increase in the probability and magnitude of harm is only slightly more than minimal risk, any potential harms associated with the procedure will be transient

and reversible in consideration of the nature of the harm, and there is no or an extremely small probability that subjects will experience significant pain, discomfort, stress or harm.

Research is "vitally important" if there is clear and significant evidence that the use of such a procedure or intervention presents a reasonable opportunity to further the understanding of the etiologist, prevention, diagnosis, pathophysiology, or alleviation or treatment of a condition or disorder.

The Principal Investigator must provide sufficient safety and efficacy data to the IRB in order for the IRB to determine whether the research interventions or procedures present only a minor increase over minimal risk. Such data is especially critical for research in which there is no prospect of direct benefit.

The IRB shall have discretion to determine whether such procedures are appropriately classified for a given research population, since the serious medical, neurological and psychiatric illnesses that give rise to impaired consent capacity may also place these individuals at an increased risk of harm and discomfort from research participation as compared to a healthy population.

The IRB will especially scrutinize any research protocols that are designed to provoke symptoms, to withdraw subjects rapidly from therapies ("wash-out"), or to use placebo controls.

ADDITIONAL SAFEGUARDS

The IRB will assess the level of risk and likelihood of direct benefit that the research offers to the research subject to assess the amount and scope of any additional safeguards for the research population. The higher the risk or the less prospect of direct benefit, the more protections will be required.

Protective measures include, but are not limited to, independent consent monitors ("ICMs") and medically responsible clinicians ("MRCs").

- An ICM is an individual not affiliated with the research who is designated by the IRB to monitor the informed consent process. The IRB may determine the role and responsibilities of the ICM, from monitoring the informed consent process to advocating on behalf of potential and current research subjects.

- A MRC is a licensed medical doctor who is skilled and experiences in working with the research population and is not affiliated with the research, who acts as an active advocate for cognitively-impaired research subjects.

The IRB will require researchers employing surrogate consent to use ICMs and MRCs for (1) any study involving more than a minor increase over minimal risk or (2) any study involving a minor increase over minimal risk with no prospect of direct benefit. The IRB will usually require use of ICMs and MRCs for any study involving a minor increase over minimal risk with the prospect of direct benefit. In all other cases, the IRB shall consider whether the use of ICMs and MRCs is necessary or appropriate to safeguard the interests of the research population.

IRB COMPOSITION

An IRB that reviews research which is expected to enroll individuals who lack or who may lack capacity must include at least one individual who is an expert in the area of research and at least one individual who is knowledgeable about or experienced in working with the relevant population. The IRB may also consider consulting with a member of the relevant population, a family member of such persons, or a representative of an advocacy group for the research population.

REQUIRED SUBMISSIONS TO THE IRB

The Principal Investigator must describe in the submission to the IRB whether the research is expected to enroll individuals who lack or who may lack capacity to provide informed consent. If so, the Principal Investigator must specify:

- The research population and the justification for the use of these individuals as the least burdened population and for specific institutional settings, if any.
- The process by which capacity would be assessed and by whom. Such process may include involvement of ICMs, or a justification for why assessment may not be required for a given research population. See Determination of Decision-Making Capacity.
- The process by which legal authority of surrogates will be verified. See *Legally Authorized Representatives*.
- The process by which prospective subjects and, if necessary, the Legally Authorized Representative, will be informed about any capacity assessment, determination, consequence of such determination (including whether it will be documented in the individual's medical record), the identity of a surrogate, the nature of the research, and the opportunity to assent, to the extent compatible with the subject's understanding, prior to enrollment. See *Notification and Assent of Subjects Who Lack Capacity*.
- An appropriate monitoring plan that:
    - Describes how capacity will be monitored throughout the duration of the study, including a plan for obtaining re-consent by the subject (if any subject is reasonably expected to regain capacity) or by an Legally Authorized Representative (if any subject is reasonably expected to lose capacity), or why such processes may not be required for a given research population;
    - Minimizes risks and negative impact on the subject's well-being, which may include involvement of MRC and must require regular communication with the Legally Authorized Representative; and
    - Requires that subjects who appear to be unduly distressed must be withdrawn from the research in a manner consistent with good clinical practice.

DETERMINATION OF DECISION-MAKING CAPACITY OF DECISION-MAKING CAPACITY

The method used to assess capacity should be tailored to the research population, the level of study risk, and the likelihood that the study will involve subjects with impaired consent capacity, and should be in accordance with applicable law. In general, the IRB considers individuals who are unable to consent for their own clinical care to be unable to consent to participate in research.

For research conducted in New York State, the IRB will require investigators to consult with a licensed physician(s) who shall perform the capacity assessment in accordance with applicable law. In general, the individual performing the assessment should be a clinician familiar with the relevant population and qualified to assess and monitor capacity of such subjects on an ongoing basis. Ideally, the individual performing the assessment should not be otherwise involved in the research. The IRB will consider the qualifications of the proposed individual(s) and whether he or she is sufficiently independent of the research team. Where the reason for lack of capacity is mental illness, New York State law requires that a psychiatrist or licensed psychologist document this determination in the individual's medical record in a signed and dated progress note [New York State Public Health Law 2994-C].

For research conducted outside of New York State, determination of capacity will be considered by the IRB in accordance with applicable local law.

For research in which recruitment of individuals with impaired consent capacity is not expected at the time of IRB submission, judgment that prospective subjects have the capacity to consent to the research can ordinarily be made informally during routine interactions with the individual during the consent process. An investigator who questions a prospective subject's capacity to consent may not enroll the individual and should consult with the IRB.

LEGALLY AUTHORIZED REPRESENTATIVES

Surrogate consent may only be provided by a subject's "Legally Authorized Representative." A Legally Authorized Representative is an individual or judicial or other body authorized under applicable local law to consent on behalf of a prospective subject to the subject's participation in the procedures involved in the research.

In New York State, the following persons are considered Legally Authorized Representatives who may act as a surrogate under this Policy, in order of priority:

- A court-appointed Legally Authorized Representative/guardian or a guardian authorized to decide about health care pursuant to Article 81 of the Mental Hygiene Law.
- An individual who is designated as a representative/agent through a health care proxy signed by both the subject and the appointed representative/agent. For a health care proxy to be effective, it must have been signed at a time when the subject had decision-making capacity. In addition, the health care proxy must not specifically prohibit research.
- The spouse, if not legally separated from the subject, or domestic partner.
- A son or daughter 18 years of age or older.
- A parent.
- A sibling 18 years of age older.
- A step-child, step-sibling, step-parent, grandparent or grandchild 18 years of age or older who has maintained such regular contact with the subject as to be familiar with the subject's activities, health or beliefs.

The IRB shall have discretion to limit the classes of persons who may act as the Legally Authorized Representative for a given study, given that each class of persons may have varying degrees of understanding of the wishes of the impaired individual regarding research participation. In general, the riskier the research protocol and more remote the prospect of direct benefit, the closer (by kinship or intimacy level) the Legally Authorized Representative should be to an impaired individual in order to consent to the impaired individual's participation in research.

The person highest on the priority list who is willing, competent and available shall be the surrogate, unless that person designates another person from the list and no one higher on the priority list than the newly-designated person objects.

The Principal Investigator shall describe how he or she will verify the legal authority of any surrogate.

The relationship of the surrogate to the individual must be documented on the signed informed consent form.

For research conducted outside of New York State, the categories of persons who may act as Legally Authorized Representatives will be considered by the IRB in accordance applicable state or local law.

NOTIFICATION AND ASSENT OF SUBJECTS WHO LACK CAPACITY

The Principal Investigator must describe in the submission to the IRB the process by which prospective subjects and, if necessary, the Legally Authorized Representative, will be informed about any capacity assessment to be performed, the results of the assessment, and any consequences of a determination of incapacity. Such notice to the prospective subject shall include the identity of a surrogate should the assessment determine lack of capacity, the nature of the research, and the opportunity to assent. The IRB shall require assent to the extent and in a manner compatible with the prospective subject's understanding.

If the prospective subject objects to the capacity determination, proposed surrogate, or decision to participate in research, such person may not be enrolled in the research unless otherwise required by law.

Once enrolled, no subject shall be required to continue to take part in research over his/her objection at any point, unless specifically authorized by a court of competent jurisdiction. Any early withdrawal of a subject shall be done in a manner consistent with good clinical practice.

ADDITIONAL CONSIDERATIONS

SUBJECTS WHOSE CAPACITY MAY CHANGE AFTER ENROLLMENT

Individuals who lack capacity to consent should be included in the process of consent to the extent possible. The IRB shall require assent to the extent and in a manner compatible with the prospective subject's understanding.

For some research populations, decision-making capacity may be reasonably expected to change during the course of the research study.

The Principal Investigator is always responsible for assessing the decision-making capacity of subjects enrolled in any research study.

If a subject unexpectedly loses capacity after enrollment, and the IRB has not prospectively approved a monitoring plan to address this circumstance, the Principal Investigator must notify the IRB. See *Required Reports to the IRB*. In most cases, the IRB will require re-consent by a Legally Authorized Representative in order for the subject to continue to participate in the research.

For research involving subjects who have capacity to provide informed consent at the time of enrollment but who may be reasonably expected to lose such capacity during the course of the research study, the Principal Investigator must submit to IRB a plan that addresses how capacity will be monitored and establishes safeguards to protect the welfare of the subject should he or she lose capacity. As part of this plan, the IRB may require that investigators establish and maintain ongoing communication with involved caregivers who could act as Legally Authorized Representatives. The IRB may require re-consent by a Legally Authorized Representative in order for the subject who has lost capacity to continue to participate in the research, especially when circumstances significantly change the potential benefits or risks or when new scientific information becomes available. When re-consent by a Legally Authorized Representative is required but not obtained, the subject must be withdrawn from the study in a manner consistent with good clinical practice.

For research involving subjects who may be reasonably expected to regain capacity during the course of the research study, the Principal Investigator must submit to IRB a plan that addresses how capacity will be monitored and establishes how re-consent by the subject will be sought if he or she regains capacity. A subject who regains capacity must re-consent in order to remain in the study. Such re-consent process must disclose all research procedures performed to date and all research procedures that remain to be performed, and allow the subject the opportunity to continue in or withdraw from the study. The subject must sign the informed consent document. If not, the subject must be withdrawn from the study in a manner consistent with good clinical practice.

SUBJECTS WITH DECISIONAL IMPAIRMENT WHO ARE DETERMINTED TO HAVE SUFFICIENT CAPACITY TO CONSENT

The NYU Langone Health IRBs recognize that decisional capacity varies along a continuum, and that the ability to provide voluntary and informed consent to participate in research may depend on factors that are specific to each protocol, such as protocol design, risks, anticipated benefits and safeguards. If appropriate, the IRB may require a Principal Investigator to include steps in the informed consent process in order to enable persons with some decisional impairment to make voluntary and informed decisions to consent to (or to refuse participation in) research, such as:

- Involvement of a trusted individual in the decision-making process.
- Allocation of additional time for the consent process.
- Waiting periods after initial discussion before enrollment.
- Repetitive teaching.
- Oral or written recall tests to assess subject understanding.
- Audiovisual presentations.
- Group sessions.
- Videotaping or audio-taping of consent interviews.
- Use of independent consent monitors to observe the consent process.

12. COMPLAINTS, NON-COMPLIANCE AND SUSPENSION OR TERMINATION OF IRB APPROVAL OF RESEARCH

12.1 COMPLAINTS

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

Complaints reported to the NYU Langone Health IRB will be evaluated as possible Unanticipated Problems involving risks to subjects or others under Section 8.8: Reportable New Information.

A Chair of the IRB and the Senior Director, HRP will promptly handle (or delegate staff to handle) and, if necessary, investigate all complaints, concerns, and appeals received by the NYU Langone Health IRBs. This includes complaints, concerns, and appeals from investigators, research subjects and others.

All complaints, written or verbal (including telephone complaints), and regardless of point of origin, are recorded and forwarded to the IRB Chair and Senior Director, HRP.

Upon receipt of the complaint, the IRB Chair will ensure that the complaint is logged and make a preliminary assessment whether the complaint warrants immediate suspension of the research project. If a suspension is warranted, the procedures in Suspension will be followed.

If the complaint alleges non-compliance with any regulations and policies described in this Policy and/or failure to follow the IRB's determinations, it will be considered an allegation of non-compliance according to Non-Compliance. If the complaint meets the definition of an Unanticipated Problem involving risk to subjects or others, it will be handled according to Section 8.8: Reportable New Information.

Any external IRB that is duly authorized to review NYU Langone Health research must follow its own procedures for review and notification to NYU Langone Health of allegations of non-compliance, as well as the applicable terms of the IRB reliance agreement.

12.2 NON-COMPLIANCE

All members of the NYU Langone Health community who are involved in human subjects research are expected to comply with the highest standards of ethical and professional conduct in accordance with federal and state regulations and institutional and IRB policies governing the conduct of research involving human

subjects. Investigators and their study staff are required to report instances of possible non-compliance. The Principal Investigator is responsible for reporting any possible non-compliance by study personnel* to the IRB. Common reports to the IRB that are not serious or continuing are typically protocol violations. However, any individual or employee may report observed or apparent instances of non-compliance to the IRB. In such cases, the reporting party is responsible for making these reports in good faith, maintaining confidentiality and cooperating with any IRB and/or institutional review of these reports.

If an individual, whether an investigator, study staff or other, is uncertain whether there is cause to report non-compliance, he or she may contact the IRB Chair directly to discuss the situation informally.

Reports of non-compliance must be submitted to IRB Operations within ten (10) working days of discovery of the alleged non-compliance. The report must include a complete description of the non-compliance, the personnel involved, and a description of the non-compliance.

Non-compliance or allegations of non-compliance that are reported to the NYU Langone Health IRB will be evaluated as Reportable New Information and possible Unanticipated Problems involving risks to subjects or others under Section 8.8: Reportable New Information.

Complainants may choose to remain anonymous.

> *Study personnel include the Principal Investigator and any staff member directly involved with subjects or the informed consent process.

DEFINITIONS

NON-COMPLIANCE means failure to comply with any of the regulations and policies described in this Policy manual and failure to follow the determinations of the IRB. Non-compliance may be minor or sporadic or it may be Serious or Continuing.

SERIOUS NON-COMPLIANCE means failure to follow any of the regulations and policies described in this Policy manual or failure to follow the determinations of the IRB and which, in the judgment of either the IRB Chair or the convened IRB, increases risks to subjects, decreases potential benefits, or compromises the integrity of the human research protections. Examples of Serious Non-Compliance include: research being conducted without prior IRB approval; and participation of subjects in research activities without their prior consent (in studies where consent was not specifically waived by the IRB). A single instance of Non-Compliance may be determined to be Serious Non-Compliance.

CONTINUING NON-COMPLIANCE means a pattern of Non-Compliance that, in the judgment of the IRB Chair or convened IRB, suggests a likelihood that instances of Non-Compliance will continue without intervention. Continuing Non-Compliance includes failure to respond to request to resolve an episode of Non-Compliance. Generally, Non-Compliance is not considered "continuing" upon initial reports or audits identifying Non-Compliance but is typically found only after repeated Non-Compliance findings.

ALLEGATION OF NON-COMPLIANCE means an unproven assertion of Non-Compliance.

FINDING OF NON-COMPLIANCE means an allegation of Non-Compliance that is proven true or a report of Non-Compliance that is clearly true. (For example, a finding on an audit of an unsigned consent document, or an admission of an investigator that the protocol was willfully not followed would represent reports of Non-Compliance that would require no further action to determine their truth, and would therefore represent findings of Non-Compliance.) Once a finding of Non-Compliance is proven, it must be categorized as Serious, non-serious, or Continuing.

IRB REVIEW OF ALLEGATIONS OF NON-COMPLIANCE

Upon receipt of a report of non-compliance or alleged non-compliance, the event will be assessed to determine the level of review required. Reports may be reviewed by an IRB Senior Manager who may either make a determination as a designee of the IRB Chair or may determine that the event must be referred to a convened IRB. All allegations of Non-Compliance that are brought to the IRB will be reviewed by the IRB Chair and the Senior Director, HRP. They will review:

- all documents relevant to the allegation;
- the last approval letter from the IRB;
- the last approved IRB application and protocol;
- the last approved consent document;
- the last approved investigator's brochure, if applicable;
- the associated grant (if applicable); and
- any other pertinent information (e.g., questionnaires, DSMB reports, etc.).

The IRB Chair and the Senior Director, HRP will review the allegation and make a determination as to the truthfulness of the allegation. They may request additional information or an audit of the research in question.

When, upon review of the information and/or results of an audit of the research in question, the IRB Chair and Director determine that Non-Compliance did not occur because the incident was within the limits of an approved protocol for the research involved, the determination is reported in writing to the Principal Investigator and, if applicable, the reporting party. The determination letter will be copied to the IO in cases where the IO and any other parties had been notified at the outset.

If, in the judgment of the IRB Chair and Senior Director, HRP, the reported allegation of Non-Compliance is not true, no further action will be taken. If, in the judgment of the IRB Chair and Senior Director, HRP, the reported allegation of Non-Compliance is true, the Non-Compliance will be processed according to Review of Findings of Non-Compliance.

If, in the judgment of the IRB Chair and Senior Director, HRP, any allegation or findings of Non-Compliance warrants suspension of the research before completion of any review or investigation to ensure protection of the rights and welfare of subjects, the IRB Chair may suspend the research as described in below in Suspension or Termination with subsequent review by the IRB.

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

REVIEW OF FINDINGS OF NON-COMPLIANCE

If, in the judgment of the IRB Chair and Senior Director, HRP, the reported finding of Non-Compliance is not Serious, not Continuing, and the proposed corrective action plan seems adequate, no further action is required and the IRB is informed at the next convened meeting. Otherwise, the matter will be presented to the IRB at a convened meeting with a recommendation that a formal inquiry (described below) will be held.

All findings of Non-Compliance referred to the IRB will be reviewed at a convened meeting. All IRB members will receive:

- all documents relevant to the allegation;
- the last approval letter from the IRB;
- the last approved IRB application; and

- the last approved consent document.

At this stage, the IRB may:

- find that there is no issue of Non-Compliance;
- find that there is Non-Compliance that is neither Serious nor Continuing and an adequate corrective action plan is in place;
- find that there may be Serious or Continuing Non-Compliance and direct that a formal inquiry (described below) be held; and/or
- request additional information.

INQUIRY PROCEDURES

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

- subjects' complaint(s) that rights were violated;
- report(s) that the Principal Investigator or other investigator is not following the protocol as approved by the IRB;
- unusual and/or unexplained adverse events in a study;
- FDA audit report of an investigator; or
- repeated failure of the Principal Investigator to report required information to the IRB.

A subcommittee is appointed consisting of IRB members, and non-members if appropriate, to ensure fairness and expertise. The subcommittee is given a charge by the IRB, which can include any or all of the following:

- review of protocol(s) in question;
- review of FDA or sponsor audit report of the investigator, if appropriate;
- review of any relevant documentation, including consent documents, case report forms, subject's investigational and/or medical files etc., as they relate to the investigator's execution of her/his study involving human subjects;
- interview of appropriate personnel if necessary;
- preparation of either a written or oral report of the findings, which is presented to the full IRB at its next meeting; and/or
- recommend actions if appropriate.

FINAL REVIEW

The results of the inquiry will be reviewed at a convened IRB meeting where the IRB will receive a report from the subcommittee. If the results of the inquiry substantiate the finding of Serious or Continuing Non-Compliance, the IRB's possible actions could include, but are not limited to:

- mandate completion of custom in-service sessions designed to specifically address the issues discovered during audit
- request a corrective action plan from the Principal Investigator;
- verification that subject selection is appropriate and observation of the actual informed consent;
- an increase in data and safety monitoring of the research activity;
- request a directed audit of targeted areas of concern;
- request a status report after each subject receives intervention;
- modify the continuing review cycle;
- request additional Principal Investigator and staff education;
- notify current subjects, if the information about the Non-Compliance might affect their willingness to continue participation;
- require modification of the protocol;
- require modification of the information disclosed during the informed consent process;

- requiring current subjects to re-consent to participation;
- suspend the study (see below); and/or
- terminate the study (see below).

In cases where the IRB determines that the event of Non-Compliance also meets the definition of Unanticipated Problem involving risks to subjects or others, the Policy and Procedure for review of such events will also be followed.

The Principal Investigator is informed of the IRB determination and the basis for the determination in writing and is given a chance to respond. If the IRB determines that the Non-Compliance was Serious or Continuing, the results of the final review will be reported as described below in Reporting.

ADDITIONAL ACTIONS

A finding of Serious or Continuing Non-Compliance may also result in the following sanctions, among others:

- suspension or termination of IRB approval of specific research protocols or of all research involving human subjects in which the investigator participates;
- sponsor actions: in making decisions about supporting or approving applications or proposals covered by this Policy, the DHHS or sponsoring agency may take into account, in addition to all other eligibility requirements and program criteria, factors such as whether the applicant has been subject to a termination or suspension as described above, and whether the applicant or the person or persons who would direct or has/have directed the scientific and technical aspects of an activity has/have, in the judgment of the DHHS or agency, materially failed to discharge responsibility for the protection of the rights and welfare of human subjects;
- OHRP and/or FDA action against the institution or individual(s). The OHRP and/or the FDA may:
  - withhold approval of all new studies by the IRB;
  - direct that no new subjects be added to any ongoing studies;
  - terminate all ongoing studies, except when doing so would endanger the subjects; and/or
  - notify relevant state, federal and other interested parties of the violations.
- individual disciplinary action of the Principal Investigator or other personnel involved in a study, up to and including dismissal, pursuant to institutional policies and procedures.

Failure to secure necessary NYU Langone Health IRB approval before commencing human subjects research must be reported to the appropriate Dean for Research for disciplinary action.

NYU Langone Health investigators should also be aware that, in general, they are indemnified under NYU Langone Health policies from liability for Adverse Events that may occur in NYU Langone Health studies approved by the NYU Langone Health IRB. Failure to follow approved procedures may compromise this indemnification and make the investigator personally liable in such cases.

12.3 SUSPENSION OR TERMINATION OF A STUDY

The IRB has the 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. Suspension of IRB approval is a directive of the convened IRB or IRB Chair or Senior Director, HRP either to temporarily stop all previously approved research activities short of permanently stopping all previously approved research activities. Suspended protocols remain open and require continuing review. The IRB Chair or Senior Director, HRP may suspend research to ensure protection of the rights and welfare of subjects. Suspension directives made by the IRB Chair or Senior Director, HRP must be reported to a meeting of the convened IRB.

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

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

The IRB shall notify the Principal Investigator in writing of such suspensions or terminations of IRB approval and shall include a statement of the reasons for the IRB's actions and explicit terms and conditions of the suspension. The Principal Investigator will be provided with an opportunity to respond in person or in writing.

When study approval is suspended or terminated by the convened IRB or an authorized individual, in addition to directing the stop of all research activities, the convened IRB or individual ordering the suspension or termination will consider whether procedures for withdrawal of enrolled subjects are necessary to protect their rights and welfare of subjects, which may include any of the procedures listed in "*Protection of Currently Enrolled Subjects*" below.

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

In the case of study suspension, the Principal Investigator MUST continue to provide reports on Adverse Events and Unanticipated Problems to both the IRB and study sponsor just as if there had never been a suspension (i.e., all events that need to be reported during a study need to continue to be reported during the suspension period.)

> *Note: Suspension or termination of protocols approved by the IRB can also be issued by the institution's administrative officials acting outside of, and unrelated to, the IRB (i.e., not necessarily related to protecting the rights and welfare of study subjects). Such administrative actions may be made for any reason in furtherance of the institution's interest. The Principal Investigator must report any suspension or termination of the conduct of research by the institution's administrative officials to the IRB. The IRB will then determine if suspension or termination of IRB approval is warranted.*

INVESTIGATOR HOLD

A Principal Investigator may request an administrative hold on a study protocol when the Principal Investigator wishes to temporarily stop some or all approved research activities. Administrative holds are not suspensions or terminations of IRB approvals; however, the IRB may decide to suspend or terminate an IRB approval regardless of whether a Principal Investigator has requested an administrative hold.

PROCEDURES

Principal Investigator must make requests to the IRB for an administrative hold on his/her study in writing, which should include:

- a statement that they are voluntarily placing a study on administrative hold;
- a description of the research activities that will be stopped;
- proposed actions to be taken to protect current subjects; and
- actions that will be taken prior to IRB approval of proposed changes in order to eliminate apparent immediate harm.

Upon receipt of written notification from the Principal Investigator, IRB Operations staff will place the study on the IRB agenda for review.

The IRB Chair and/or Director, in consultation with the Principal Investigator, will determine whether any additional procedures need to be followed to protect the rights and welfare of current subjects as described in "*Protection of Currently Enrolled Subjects*" below. Suspensions of new enrollment pursuant to a Principal Investigator-initiated hold must be reported to the research sponsor(s).

The IRB Chair and/or Director, in consultation with the Principal Investigator, determine how and when currently enrolled subjects will be notified of the administrative hold.

A Principal Investigator may request a modification of the administrative hold by submitting a request for a modification to previously approved research.

PROTECTION OF CURRENTLY ENROLLED SUBJECTS

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

- transferring subjects to another investigator participating in the study;
- making arrangements for clinical care outside the research;
- allowing continuation of some research activities under the supervision of an independent monitor;
- requiring or permitting follow-up of subjects for safety reasons;
- requiring Adverse Events or outcomes to be reported to the IRB and the study sponsor;
- notification of current subjects; or
- notification of former subjects.

12.4 REPORTING

Serious or Continuing Non-Compliance, Unanticipated Problems posing risks to subjects or others and suspensions or terminations of IRB approvals must be reported to the appropriate regulatory agencies and institutional officials according to the procedures in Reporting to Regulatory Agencies and Institutional Officials.

13. REPORTING TO REGULATORY AGENCIES AND INSTITUTIONAL OFFICIALS

For applicable studies, federal regulations require prompt reporting to appropriate institutional officials, and government oversight agencies of (i) any Unanticipated Problems involving risks to subjects or others, (ii) any Serious or Continuing Non-Compliance or (iii) any suspension or termination of IRB approval. The NYU Langone Health IRB will comply with this requirement and the following procedures describe how these reports are handled.

IRB Operations will initiate these reporting procedures as soon as the IRB takes any of the following actions:

- determines that an event may be considered an Unanticipated Problem involving risks to subjects or others;
- determines that Non-Compliance was Serious or Continuing; and/or
- suspends or terminates IRB approval of research.

IRB Operations staff (manager, senior specialist, or specialist) will prepare a letter that contains the following information:

- the nature of the event (Unanticipated Problem involving risks to subjects or others, Serious or Continuing Non-Compliance, suspension or termination of IRB approval of research);
- name of the institution conducting the research;
- title of the research project and/or grant proposal in which the problem occurred;
- name of the Principal Investigator on the protocol;
- number/identifier of the research project assigned by the NYU Langone Health IRB and the number of any applicable federal award(s) (e.g., grant, contract, or cooperative agreement);
- a detailed description of the problem including the findings of the organization that conducted an audit/investigation of the alleged Non-Compliance and the reasons for the IRB's decision;
- actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.); and
- plans, if any, to send a follow-up or final report by the earlier of a specific date when an investigation has been completed or a corrective action plan has been implemented.

The IRB Chair and the Senior Director, HRP will review the letter and modify the letter as needed.

The Senior Director, HRP will sign the letter and return it to IRB Operations, which sends a copy of the report to:

- the IRB by including the letter in the next agenda packet as an information item;
- the IO;
- OHRP, if the study is subject to DHHS regulations or subject to a DHHS federal wide assurance (FWA);
- the 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 Principal Investigator, study sponsor, another institution, or other mechanisms.
- the Principal Investigator;
- department chair 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 of that Covered Entity;
- the information security officer of an organization if the event involved violations of information security requirements of that organization;
- the applicable office of risk management; and
- others as deemed appropriate by the IO (e.g., SPA).

The Senior Director, HRP ensures that all steps of this Policy are completed within ten (10) days of the initiating action whenever feasible. For more serious actions, the Senior Director, HRP will expedite reporting.

14. INVESTIGATIONAL DRUGS & DEVICES IN RESEARCH

The following procedures describe the use of investigational drugs and devices in research conducted under the auspices of NYU Langone Health. Use of investigational drugs must be conducted according to FDA IND regulations, [21 CFR Part 312], other applicable FDA regulations, and institutional policies. Use of an investigational device in a Clinical Trial to obtain safety and effectiveness data must be conducted

according to FDA's IDE regulations, [21 CFR Part 812], and other applicable FDA regulations. The IRB will provide written documentation of approval to the Principal Investigator with a determination of whether the investigational device presents a significant or non-significant risk as used in the research.

14.1 DEFINITIONS

Investigational Drug means an investigational drug for clinical research use is one for which the Principal Investigator or a sponsor has filed an IND application [21 CFR Part 312], or an FDA-approved drug that is being studied for an unapproved or approved use in a controlled, randomized, or blinded Clinical Trial.

INVESTIGATIONAL DEVICE means a medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. As further stated, a "medical device" is any healthcare product that does not achieve its principal intended purpose by chemical action or by being metabolized. The Investigational Device Exemption (IDE) regulations [21 CFR part 812] describes two types of device studies; "significant risk" (SR) and "non-significant risk" (NSR).

INVESTIGATIONAL NEW DRUG (IND) means an Investigational New Drug application in accordance with [21 CFR Part 312].

INVESTIGATIONAL DEVICE EXEMPTION (IDE) means an Investigational Device Exemption in accordance with [21 CFR 812].

EMERGENCY USE refers to the use of 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 IRB approval [21 CFR 56.102(d)].

TEST ARTICLE means any drug, biological product, or medical device for human use [21 CFR 56.102(1)].

SIGNIFICANT RISK (SR) DEVICE means [21 CFR 812.3(m)] a medical device that presents a potential for serious risk to health, safety, or welfare of a subject and

- is intended as an implant;
- is used in supporting or sustaining human life;
- is of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise prevents impairment of human health; and
- otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

NON-SIGNIFICANT RISK (NSR) DEVICE means an investigational medical device that does not meet the definition for a significant risk device.

HUMANITARIAN USE DEVICE (HUD) means a device intended to benefit patients by treating or diagnosing a disease that affects fewer than 8,000 individuals in the United States per year.

14.2 FDA EXEMPTIONS

The following categories of clinical investigations are not regulated by DHHS or any other federal agency and are exempt from the requirements of FDA regulations for IRB review:

EMERGENCY USE OF A TEST ARTICLE

Emergency use of a Test Article is exempt from prior IRB review and approval, provided that such emergency use is reported to the IRB within five (5) working days. Any subsequent use of the Test Article

at the institution is subject to IRB review. [21 CFR §56.104(c)] Tracking of use of a Test Article at NYU Langone Health is a shared responsibility of IRB Operations and RABO.

TASTE AND FOOD QUALITY EVALUATIONS AND CONSUMER ACCEPTANCE STUDIES

If wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. [21 CFR §56.104(d)]

14.3 IND/IDE REQUIREMENTS

When the principal intent of the investigational use of a Test Article is to develop information about the product's safety or efficacy, an Investigational New Drug (IND) or Investigational Device Exemption (IDE) may be required.

Investigators will be asked through the IRB application to indicate whether the research involves drugs or devices. If so, they will be asked if there is an IND/IDE for the research. If there is, they will be asked for evidence of the IND/IDE, which could be in the form of:

- an industry sponsored protocol with IND/IDE;
- a letter from FDA;
- a letter from industry sponsor; and/or
- other document and/or communication verifying the IND/IDE.

Note: An IND goes into effect thirty (30) days after the FDA receives the IND, unless the sponsor receives earlier notice from the FDA.

If the research involves drugs or devices and there is no IND/IDE, the Principal Investigator must provide a rationale why it is not required. The rationale could be in the form of:

- a letter from FDA;
- protocol with justification for exemption from IND/IDE (as applicable); and/or
- a letter from an industry sponsor (or investigator-sponsor).

For studies involving drugs, an IND may not be necessary if all of the following conditions are met (21 CFR 312.2(b)(1)):

- The drug or drugs being studied in the research is lawfully marketed in the United States;
- The research is not intended to be reported to the FDA as a well-controlled study in support of a new indication for use or to support any other significant change in the labeling for the drug;
- The research is not intended to support a significant change in the advertising for the product;
- the research does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
- The research is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50], respectively;
- The research is conducted in compliance with the requirements concerning the promotion and sale of drugs [21 CFR 312.7]; and
- The research does not intend to invoke [21 CFR 50.24]: exception from informed consent requirements for emergency research.

For clinical investigations involving an in vitro diagnostic biological product (i.e., one or more of the following: (a) blood grouping serum, (b) reagent red blood cells, or (c) anti-human globulin), an IND is not necessary if:

(a) it is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and

(b) it is shipped in compliance with 21 CFR 312.160.

If the research is a clinical investigation involving use of a placebo and does not otherwise require submission of an IND, an IND is not necessary.

For studies involving Medical Devices, an IDE may not be necessary if any of the following conditions are met:

- There is a claim that the device is a non-significant risk device (NSR);
- The research involves a device other than a transitional device, in commercial distribution immediately before May 28, 1976 when used or investigated in accordance with the indications in labeling in effect at that time;
- The research involves a device other than a transitional device, in commercial distribution immediately before May 28, 1976 that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of [21 CFR 807] in determining substantial equivalence;
- The research involves a diagnostic device, if the sponsor complies with applicable requirements in [21 CFR 809.10(c)] and if the testing:
    - is noninvasive;
    - does not require an invasive sampling procedure that presents significant risk;
    - does not by design or intention introduce energy into a subject; and
    - is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.
- The research involves a device undergoing consumer preference testing, testing of a modification, testing of a combination of two or more devices in commercial distribution, or if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk;
- The research involves a device intended solely for veterinary use;
- The research involves a device shipped solely for research on or with laboratory animals and labeled in accordance with [21 CFR 812.5(c)]; or
- The research involves a custom device as defined in [21 CFR 812.3(b)], unless the device is being used to determine safety or effectiveness for commercial distribution.

If a sponsor (or investigator-sponsor) has identified a study as a NSR device study, then the Principal Investigator must provide an explanation of the NSR determination, which could be in the form of:

- an industry protocol with NSR justification;
- a letter from the FDA; or
- a letter from the study's industry sponsor, if applicable (or investigator-sponsor).

A study may be determined to be an NSR device study based on any of the following criteria:

- The device being studied is not intended as an implant that presents a potential for serious risk to the health, safety, or welfare of a subject;

- The device being studied is not purported or represented to be for use in supporting or sustaining human life and does not present a potential for serious risk to the health, safety, or welfare of a subject;
- The device being studied is not for use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and does not present a potential for serious risk to the health, safety, or welfare of a subject; or
- The device being studied does not otherwise present a potential for serious risk to the health, safety, or welfare of a subject.

If the FDA has determined that the study is a NSR device study, documentation of that determination must be provided.

ABBREVIATED IDE REQUIREMENTS

For Investigational Devices, NSR device studies follow abbreviated IDE requirements and are not required to have to have an IDE application approved by the FDA.

Under the abbreviated IDE requirements, the following categories of investigations are considered to have approved applications for IDE's, unless the FDA has notified a sponsor under 21 CFR 812.20(a) that approval of an IDE application is required:

> (1) An investigation of a device other than a significant risk (SR) device, if the device is not a banned device and the sponsor (or sponsor-investigator):
> (i) Labels the device in accordance with 21 CFR 812.5;
> (ii) Obtains IRB approval of the investigation after presenting the reviewing IRB with an explanation of why the device is not a significant risk device, and maintains such approval;
> (iii) Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent under 21 CFR Part 50 and documents such informed consent, unless documentation is waived by an IRB under 21 CFR 56.109(c);
> (iv) Complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations of Investigational Devices;
> (v) Maintains the records required under 21 CFR 812.140(b) (4) and (5) and makes the reports required under 21 CFR 812.150(b) (1) through (3) and (5) through (10);
> (vi) Ensures that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 21 CFR 812.150(a) (1), (2), (5), and (7); and
> (vii) Complies with the prohibitions in 812.7 against promotion and other practices.

If there is no submission to the FDA, IRB Operations staff will confirm that sufficient documentation is provided to demonstrate that the study meets NSR criteria or qualifies for one of the exemptions from IND/IDE requirements (as applicable).

The IRB will then review the IRB application and, based upon the documentation provided, determine: (a) that there is an approved IND/IDE in place, (b) that the FDA has determined that an IND is not required or that the study is exempt or is a NSR device study, or (c) if neither of the above, whether or not an IND/IDE is necessary, or that the device study is exempt or is a NSR device study, using the criteria above. In cases when the IRB determines a study does not meet the proposed IND/IDE exemption or NSR criteria, the IRB will require submission to the FDA. The FDA will make the determination and is the final arbiter. The IRB

will not grant approval to the research until the IND/IDE status is determined, and, if necessary, an approved IND or IDE is in place.

14.4 INVESTIGATOR-SPONSORS

In reviewing research involving FDA-regulated Test Articles, the IRB will determine if the study will be conducted under an NYU Langone Health investigator-sponsor. If so, the IRB will inform the Principal Investigator that there are sponsor responsibilities applicable to IND or IDE studies, including reporting requirements to the FDA, (as well as the Principal Investigator responsibilities) and that all these requirements are his/her responsibility. The Principal Investigator is directed to the *NYU Langone Health IRB Guidance for Special Considerations for the Oversight of Research Protocols* in FDA-regulated Drug or Device Studies.

Staff from the NYU Langone Health Office of Research Regulatory Affairs – Research Regulatory Services will visit the investigator-sponsor before initiation of the research to determine compliance with these FDA regulatory requirements. If compliance has been demonstrated, the investigator-sponsor may begin the research. The Research Regulatory Services staff will evaluate whether the Principal Investigator is knowledgeable about the regulatory requirements of sponsors and will follow them. An internal audit of the study will take place after the enrollment of the first two (2) subjects in such study.

If the research involves drugs or devices and there is no IND/IDE, the investigator will be asked for a rationale as to why it is not required.

IRB Operations will conduct education programs for Principal Investigators holding an IND or IDE on the applicable regulations.

The IRB will review the IRB application and determine:

- whether there is an IND/IDE and if so, whether there is appropriate supporting documentation; and
- if there are drugs or devices involved, but no IND/IDE, whether the research meets the above criteria.

14.5 RESPONSIBILITIES IN RESEARCH OF INVESTIGATIONAL DRUGS AND DEVICES

PRINCIPAL INVESTIGATOR

The Principal Investigator is responsible for ensuring that the drug/device research is conducted according to all regulatory requirements, guidelines, and IRB and institutional policies and procedures, including obtaining approval from the IRB. For studies where the Principal Investigator files for and conducts a study under an IND or IDE, the Principal Investigator is considered the sponsor-investigator and as such carries all of the FDA regulatory responsibilities and reporting obligations of both the Principal Investigator and the sponsor as described in the FDA regulations.

The Principal Investigator proposing the drug/device research will be required to provide a research plan that will be evaluated by the IRB, which should include the plan for:

- drug/device storage;
- maintaining security of the drug/device; and
- dispensation of the drug/device.

The Principal Investigator is responsible for the accountability of Investigational Drug/Device including receipt, storage, security, dispensation, administration, return, disposition, and keeping Investigational

Drug/Device accountability records. The Principal Investigator may delegate the responsibility for drugs/device/biologic accountability to responsible staff of an investigational pharmacy.

If, because of special circumstances, an Investigational Drug is not stored in the designated investigational pharmacy, the Principal Investigator is responsible for the proper storage, security and dispensation of the Drug/Device. The Principal Investigator must complete and submit an investigational control sheet containing information on the plan for storage, security and dispensing of the drug or device to the IRB prior to its approval of the study. All Investigational Drugs and Devices received for use in a study must be stored in a secure, limited access area that is within an area of the Principal Investigator's control. Drugs require additional security; the storage area must be locked. Proper instructions on the use of the Investigational Drug or Device must be provided to the study subjects. A log must be kept regarding the receipt, use and/or dispensing of the Investigational Drug and/or Device and the disposition of remaining supplies at the conclusion of the study.

The Principal Investigator is responsible for reporting all unexpected Adverse Events associated with the use of an Investigational Drug/Device to the FDA within fifteen (15) calendar days from initial receipt of the information if the Principal Investigator is the sponsor-investigator, and to the study sponsor, as applicable, in accordance with timelines proscribed by the sponsor in the study protocol. Unexpected fatal or life-threatening Adverse Events suspected to be related to use of the Investigational Drug/Device should be reported to the FDA as soon as possible but not later than seven (7) calendar days from initial receipt of the information. All Adverse Events that require prompt reporting to the IRB must be reported according to the Section 8.8: Reportable New Information

PHARMACY NOTIFICATION AND RECORD-KEEPING REQUIREMENTS FOR RESEARCH INVOLVING INVESTIGATIONAL DRUGS

- The Principal Investigator is responsible for informing the applicable pharmacy that IRB approval has been obtained for a study involving Investigational Drugs. In addition, a signed copy of the IRB-approved consent form must be provided to the pharmacy to document each subject's consent to participate in the study prior to Investigational Drug being dispensed to such subject.

- The Principal Investigator must inform the appropriate IRB and the applicable pharmacy when a study involving Investigational Drugs has been terminated.

- Where allowed, or required, the Principal Investigator may assign some or all duties for Investigational Drug accountability at the study sites to a qualified pharmacist or another appropriate individual who is under the supervision of the Principal Investigator.

The Principal Investigator or the pharmacist, or other designated individual must maintain records of the Investigational Drug's delivery to the applicable study site, the Investigational Drug inventory at the study site, the use by each subject, and the return to the study sponsor or alternative disposition of unused Investigational Drug products. Principal Investigators should maintain records that document adequately that the subjects are provided the doses specified by the applicable protocol and reconcile the disposition of all Investigational Drug products received from the study sponsor (as applicable).

- Receipt logs are maintained for all Investigational Drugs. Documentation of the following elements (as applicable) is required for each drug used:
    - Name of drug
    - Dosage and strength
    - Lot and/or batch number
    - Date received from supplier
    - Shipment/packing slip number
    - Expiration date of drug
    - Number of boxes/kits received

- Condition of drug (intact/damaged)
- Recipient initials

- Accountability logs are maintained for all Investigational Drugs. Documentation of the following elements (as applicable) is required for each drug used:
  - Name of drug
  - Dosage and strength
  - Lot and/or batch number
  - Research subject initials (for internal tracking purposes)
  - Research subject study Identification number
  - Quantity dispensed and initials of the person who dispensed the drug
  - Disposition. If drug is returned to the sponsor/supplier or destroyed, documentation of why, when and persons involved.
  - Initials of all persons who used or disposed of each Investigational Drug

NOTIFICATION, MAINTENANCE, AND RECORD-KEEPING REQUIREMENTS FOR RESEARCH INVOLVING INVESTIGATIONAL DEVICES

For research involving Investigational Devices, the following notification and record-keeping requirements apply:

- If a device that the Principal Investigator or study sponsor considers to be NSR is determined by the IRB to be a significant risk (SR) device upon IRB review, the Principal Investigator is responsible for notifying the sponsor of the IRB's determination upon receipt of written notice, as applicable. The Principal Investigator should provide the IRB with confirmation of this action.

- A copy of the protocol approval by the FDA and the IRB as well as a copy of the IRB-approved consent form must be provided to the designated pharmacist if the Investigational Device will be stored in an investigational pharmacy. A copy of the consent from signed by the applicable research subject must be provided to the pharmacist prior to the Investigational Device being released for use. If the Principal Investigator is self-storing the devices, a log must be maintained to indicate name of each subject, date the Investigational Device was dispensed, by whom it was dispensed, amount of Investigational Devices remaining, and who received the device (see below for detailed requirements related to management of research involving Investigational Devices).

- Following completion of the study, the termination procedure for Investigational Drug studies (informing the applicable IRB and pharmacy when the study has been terminated) must be applied if the Investigational Devices are under investigational pharmacy control. If the devices are kept by the Principal Investigator, the device accountability log must be completed regarding the receipt, use and/or dispensing of the Investigational Devices, and the disposition of remaining devices at the conclusion of the investigation.

The Principal Investigator is responsible for maintaining security of the Investigational Devices by ensuring that:

- all Investigational Devices used in conjunction with the protocol are kept in a locked and secured area, separate from materials used in standard clinical care;
- access to Investigational Devices is limited to personnel designated by the Principal Investigator; and
- receipt logs are maintained for all Investigational Devices. Documentation of the following elements (as applicable) is required for each device used:
  - Name of device
  - Model number
  - Serial number

    - Lot, batch, and/or serial number
    - Date received from supplier
    - Shipment/packing slip number
    - Expiration date of the device (if applicable)
    - Condition of the device (intact/damaged)
    - Recipient initials
- accountability logs are maintained for all Investigational Devices. Documentation of the following elements (as applicable) is required for each device used:
    - Name of device
    - Model number
    - Lot, batch and/or serial number
    - Research subject initials (for internal tracking purposes)
    - Research subject study Identification number
    - Date implanted or used
    - Disposition. If device is returned to the sponsor/supplier or destroyed, documentation of why, when and persons involved.
    - Initials of all persons who received, used, or disposed of each Investigational Device.
    - Expiration date of the device

The full names, title/positions, and signatures of all personnel responsible for maintaining or documenting information in the Investigational Device accountability logs must be indicated on a separate document or on the log itself.

Device accountability logs must be maintained in the study/research files or in the Principal Investigator's study/research regulatory binder for the period of time required by the federal regulations or otherwise required by the relevant agreement/contract term, whichever is longer.

Prior to commencement of research at NYU Langone Health involving Investigational Devices, IRB Operations staff will conduct a review to evaluate compliance with aforementioned in order to affirm compliance.

For studies involving Investigational Devices, the Principal Investigator is responsible for protecting the rights, safety and welfare of research subjects under the Principal Investigator's care by ensuring that:

- the Investigational Device is not used on a research subject until FDA and/or IRB approval has been obtained and the research subject has signed an IRB-approved informed consent document;
- the research is conducted according to all regulatory requirements and guidelines;
- the Investigational Device is used only in accordance with the IRB-approved protocol;
- the Principal Investigator is thoroughly familiar with the appropriate use of the Investigational Device, as described in the protocol and product brochure, and in other informational sources provided by the sponsor/supplier;
- all persons assisting in the study are adequately informed about the protocol and the Investigational Device; and
- research subjects receive adequate instructions about the Investigational Device to assure their safe participation in the research study.

IRB RESPONSIBILITIES

The IRB must review the Investigational Drug/Investigational Device research using the same criteria it would use in considering approval of any research involving an FDA-regulated product (21 CFR 56.111), and in compliance with these Policies and Procedures.

DETERMINATION OF NON-SIGNIFICANT RISK (NSR) VS. SIGNIFICANT RISK (SR) DEVICE

For research involving Investigational Devices where there is a claim that the device is a non-significant risk (NSR) device:

- The IRB is responsible for reviewing the protocol and determining whether it is adequate. If the IRB Chair determines that the IRB does not have the necessary expertise to evaluate the investigational plan, outside consultation will be sought as appropriate (e.g., from NYU Langone Health Biomedical Engineering).
- Unless the FDA has already made a risk determination for the study, the IRB will review NSR studies and determine if the Investigational Device represents significant or non-significant risk and report its findings to the Principal Investigator in writing.
- The IRB must consider the risks and benefits of the Investigational Device compared to the risks and benefits of alternative devices or procedures. NSR device studies do not require submission of an IDE application, but must be conducted in accordance with the abbreviated requirements of IDE regulations (see *IND/IDE Requirements*). If the study that has been submitted as a NSR device study but is subsequently determined to be a SR device study, the IRB must recommend that an IDE be obtained.
- Protocols involving SR devices do not qualify for expedited review. Protocols involving NSR devices do not automatically qualify for expedited review.
- The IRB must document in the IRB meeting minutes the rationale for the determination of the risk classification of a device (as NSR or SR).
- The IRB will provide written documentation of its approval of a study to the Principal Investigator with a determination of whether the Investigational Device involved presents a significant or non-significant risk.

If the FDA has already made the SR or NSR determination for a study, the FDA's determination is final and the IRB does not need to make a risk determination.

14.6 EMERGENCY USE

HHS regulations do not permit human subjects research activities to be started, even in an emergency, without prior IRB approval. When emergency medical care with any Test Article (including Investigational Drugs or Devices) is initiated without prior IRB review and approval, the patient may not be considered a research subject under [45 CFR Part 46]. However, nothing in the HHS regulations at [45 CFR Part 46] is intended to limit the authority of a physician to provide emergency medical care with any Test Article, Investigational Drug or Investigational Device, to the extent the physician is permitted to do so under applicable federal, state or local law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe).

EMERGENCY EXEMPTION FROM PROSPECTIVE IRB APPROVAL

The FDA , in 21 CFR 56.102(d), defines "emergency use" as the use of an investigational drug or biological product with a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

If all conditions described in [21 CFR 56.102(d)] exist, then the emergency exemption from prospective IRB approval found at [21 CFR 56.104(c)] may be utilized. Informed consent is normally required and should be obtained and documented as per FDA regulations unless the conditions for exemption are met. See *Emergency Waiver of Informed Consent.*

The IRB must be notified within five (5) working days when an Investigational Drug, Investigational Device, or any other Test Article is used under the emergency exemption. Any subsequent use of the Test Article at the institution is subject to IRB review.

The IRB's acceptance of the required notification to the IRB must not be construed as its approval for the emergency use. The Senior Director, HRP or designee will review the report to verify that circumstances of the emergency use conformed to FDA regulations.

If use of an Investigational Drug, Investigational Device, or other Test Article in a patient is initiated without prior IRB review approval, the data derived from such use may not be included in DHHS-regulated research in a prior or subsequent IRB-approved study.

If use is initiated without prior IRB review and approval, the FDA may require the data from emergency use to be included in the research results submitted to the FDA.

EMERGENCY WAIVER OF INFORMED CONSENT

Under New York State law, the Principal Investigator is required to obtain informed consent from the patient or the patient's Legally Authorized Representative unless an exception is met as follows.

An exception under FDA regulations at [21 CFR 50.23] permits the emergency use of an investigational drug, device, or biologic without informed consent where the Principal Investigator and an independent physician who is not otherwise participating in the clinical investigation certify in writing all four of the following specific conditions:

- The subject is confronted by a life-threatening situation necessitating the use of the test article.
- Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject.
- There is insufficient time to obtain consent form the subject's Legally Authorized Representative.
- No alternative method of an FDA-approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

If there is not enough time to obtain the independent physician determination before use of the Test Article, the actions of the Principal Investigator must be reviewed and evaluated in writing by an independent physician within five to six (5-6) working days.

EXPANDED ACCESS OF INVESTIGATION DRUGS

The term "compassionate use" is erroneously used to refer to the provision of investigational drugs outside of an ongoing clinical trial to a limited number of patients who are desperately ill and for whom no standard alternative therapies are available. The term "compassionate use" does not, however, appear in FDA or HHS regulations. 21 CFR Subpart I, Section 312.300 explains the regulations for "Expanded Access", a mechanism for providing eligible subjects with Investigational Drugs or biologics (as early in the drug development process as possible) for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments.

The FDA defines an "immediately life-threatening" disease as a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

The FDA defines a "serious disease or condition" as one associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity are usually insufficient, but the morbidity need not be irreversible, as long as it is persistent or recurrent. The determination of whether a disease is serious is based on clinical judgment when considering factors including survival, day-to-day

functioning, or the likelihood that the disease, if left untreated, would progress from a less severe condition to a more serious one.

There are 3 requirements that must be met before Expanded Access to an Investigational Drug/biologic can be issued:

- The drug is intended to treat a serious or immediately life-threatening disease or condition and there is no comparable or satisfactory alternative treatment available;
- The potential benefit to the patient justifies the potential risks of the treatment use and those potential risks are not unreasonable in the context of the disease or condition to be treated; and
- Providing the Investigational Drug/biologic for the treatment use will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use.

FDA regulations allow certain individuals who are not enrolled in clinical trials to obtain expanded access to Investigational Drugs, agents, or biologics through the following methods:

INDIVIDUAL PATIENTS, INCLUDING EMERGENCY USE

The FDA may approve use by a licensed physician of an Investigational Drug or biologic outside of a controlled clinical trial for individual patients, usually in a desperate situation, and if the patient is unresponsive to other therapies or is in a situation where no approved or generally recognized treatment is available. The drug or biologic may or may not be under development. There is usually little evidence that the proposed therapy is useful, but may be plausible on theoretical grounds or anecdotes of success. Access to Investigational Drugs/biologics for use by a single, identified patient may be gained either through the a drug manufacturer/sponsor's existing IND under an *Individual Patient Expanded Access Protocol*, or through the FDA, by submitting a protocol for *Individual Patient Expanded Access IND* to the FDA requesting authorization to use the Investigational Drug/biologic for treatment use under a new IND and obtaining the drug from the drug manufacturer/sponsor. This type of submission is commonly referred to as a "Single Patient Protocol" or "Single Patient IND". Along with meeting the criteria in 21 CFR 312.305(a), the sponsor must determine that the probable risk to the patient from the investigational drug/biologic is not greater than the probable risk from the disease or condition.

Unless the FDA authorizes treatment to begin sooner, there is a 30-day waiting period for the Individual Patient Expanded Access IND. However, there is no waiting period for the Individual Patient Expanded Access Protocol.

Prospective IRB review and approval is required prior to initiating treatment.

Emergency IND (Individual patient access IND for emergency use) and Emergency Protocol (Individual patient expanded access protocol for emergency use):

In emergency situations when a patient requires treatment before the FDA submission can be made in writing, the FDA may authorize the use of the Investigational Drug/biologic in the patient either by telephone or other method of rapid electronic communication. Prospective IRB review and approval are required before treatment can be initiated unless the conditions for exemption are met [21 CFR 56.104(c) and 56.102(d)]. Informed consent is required unless the conditions for exemption are met (21 CFR 50.23). A licensed physician or sponsor must submit the required documents for the Emergency IND or Protocol to the

FDA within 15 business days of the FDA's telephone, facsimile, or other electronic authorization of the use of the Investigational Drug/biologic.

At the conclusion of the individual patient's treatment, the physician or sponsor must provide the FDA with a written summary of the results of the expanded access use, including adverse effects.

When a significant number of similar individual patient access/single patient IND requests have been submitted, the FDA may require the sponsor to submit an IND or protocol for intermediate-sized population or widespread expanded access.

INTERMEDIATE-SIZE PATIENT POPULATIONS

Access to an Investigational Drug or biologic for treatment can be granted to more than one patient, but fewer patients than are treated under a Treatment IND or Treatment Protocol for widespread use, either by submitting to the FDA a protocol under a new IND, subject to a 30-day waiting period (unless the FDA notifies the sponsor that treatment may begin sooner) or by submitting a protocol to an existing IND by the sponsor of the existing IND. In the latter example, there is no waiting period imposed by the FDA. However, prospective IRB review and approval are required before initiating treatment.

This method of expanded access is appropriate for the following circumstances:

- Treatment of rare diseases or conditions when the drug or biologic is not being developed due to the inability to recruit a sufficient number of patients for a clinical trial.
- In cases when the investigational drug or biologic is being tested in a clinical trial, an intermediate-size population submission may be needed when the patients do not meet the eligibility criteria for the study, the trial is closed to enrollment, or enrollment is not feasible because the trial site is not geographically accessible to the patient.
- The FDA-approved drug or biologic or related product is otherwise unavailable to patients because the drug is no longer marketed for safety reasons or because it has failed to meet the conditions of its approved application, or due to a drug shortage.
- The regulations do not specify an upper-limit for the number of patients to be treated under an intermediate-size patient population IND or protocol. However, as the number of patients increases, the FDA may require the sponsor to submit an IND or protocol for treatment use under 21 CFR 312.320.

TREATMENT IND OR TREATMENT PROTOCOL

FDA regulations [21 CFR 312.320] address the widespread treatment use of an Investigational Drug or biologic (not approved for marketing, but under clinical investigation for a serious or immediately life-threatening disease condition) in patients for whom no comparable or satisfactory alternative drug or other therapy is available. Use of the Investigational Drug or biologic for this purpose must meet all criteria for Expanded Access Use (21 CFR 312.305(a) and the FDA must have determined that:

- The drug or biologic is already under investigation to support a marketing application for the expanded access use or clinical trials have been completed; *and*
- The trial sponsor is actively pursuing marketing approval for the drug; *and*
- There is sufficient clinical evidence of safety and effectiveness from Phase 3 data or compelling Phase 2 data to support the expanded access use *OR*

- Considering the available evidence as a whole, it is reasonable to conclude that the Investigational Drug/biologic may be effective for the expanded access use and would not expose patients to an unreasonable and significant risk of illness or injury. This evidence could be based on Phase 3 or Phase 2 data as well as more preliminary clinical evidence.

Prospective IRB review and approval is required prior to this use.

INFORMED CONSENT

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

CHARGING FOR INDS UNDER EXPANDED ACCESS

The FDA permits charging for the Investigational Drug, agent, or biologic when used in an Expanded Access IND or protocol. Therefore, the IRB Committee should pay particular attention to Expanded Access IND/protocols in which the subjects will be charged for the cost of the Investigational Drugs/products. If subjects will be charged for use of the Investigational Drug/agent/biologic, economically disadvantaged persons will likely be excluded from participation. Charging for participation may preclude economically disadvantaged persons as a class from receiving access to Investigational Drug/agent/biologic. The IRB should balance this interest against the possibility that unless the manufacturer/sponsor can charge for the Investigational Drug/agent/biologic, it will not be available for treatment use until it receives full FDA approval.

EMERGENCY USE IND AND EMERGENCY WAIVER OF IND

The emergency use of an unapproved Investigational Drug, agent, or biologic requires an emergency IND. The FDA has established mechanisms and guidance for obtaining an emergency IND for the use of Investigational Drugs, agents, or biologics.

FDA regulations at [21 CFR 312.305(a)] address the need for an Investigational Drug to be used in an emergency situation that does not allow time for submission of an IND. The FDA may authorize shipment of the Investigational Drug for a specific use in such a circumstance in advance of submission of an IND. Prospective IRB review is required unless the conditions for exemption are met [21 CFR 56.104(c) and 56.102(d)]. Informed consent is required unless the conditions for exemption are met (21 CFR 50.23). All applicable regulations must be met including those at [21 CFR Parts 50 and 56], and [21 CFR 305(a)].

WAIVER OF INFORMED CONSENT FOR PLANNED EMERGENCY RESEARCH

Planned emergency research that involves the waiver of informed consent is subject to specific review and requirements. [21 CFR §50.24] The research plan must be approved in advance by the FDA or DHHS and the IRB, and publicly disclosed to the community in which the research will be conducted. Such studies are not allowed under the regulations covering the emergency use of a test article in a life-threatening situation [21 CFR § 56.104(c)]. See *Section 10.13 Waiver of Informed Consent for Planned Emergency Research*.

Planned emergency research conducted by or at NYU Langone Health that involves the waiver of informed consent is subject to the additional requirements set forth in NYU Langone Health's *Policy on Planned Emergency Research.*

EXPANDED ACCESS OF INVESTIATIONAL DEVICES

Individuals who are not enrolled in clinical trials may obtain access to Investigational Devices through the following methods:

COMPASSIONATE USE (INDIVIDUAL PATIENT/SMALL GROUP ACCESS)

The "compassionate use" mechanism allows access to Investigational Devices for patients who do not meet the requirements for inclusion in a clinical trial but for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing or monitoring the patient's disease or condition and this potential benefit justifies the potential risks of the device. This provision is typically approved for individual patients but may be also approved to treat a small group. The patient's disease must be a serious or life-threatening disease or condition with no alternative treatment available. FDA approval is needed before use of the Investigational Device under this provision.

If the Investigational Device already has an existing IDE, the IDE sponsor should submit an IDE supplement for Compassionate Use under 21 CFR 812.35(a) to treat the individual patient or small group. The IDE supplement is subject to a 30-day review cycle, although approval may be granted earlier in consideration of the need of the patient(s). After all patients have been treated, a follow-up report on the use of the Investigational Device must be submitted.

If the Investigational Device does not already have an IDE, the treating physician or device manufacturer needs to submit a compassionate use request for a single patient to the FDA. IRB review and approval are required prior to initiating use of the device. Following the compassionate use of a device, a follow-up report, including a summary of the patient outcome and any problems that occurred due to the use of the device, must be submitted by the IDE sponsor to the FDA within 45 days of using the Investigational Device. Additionally, this report must be submitted to the IRB as soon as possible.

TREATMENT USE

An approved IDE specifies the maximum number of clinical trial sites and the maximum number of human subjects that may be enrolled in the applicable study. During the course of the clinical trial, if the data suggests that the Investigational Device is effective, then the trial may be expanded to include additional subjects with life- threatening or serious diseases. The criteria for treatment use with an Investigational Device include:

- The device is intended to treat a life-threatening or serious disease.
- There is no comparable or satisfactory alternative treatment available.
- The device is already under investigation for the same use under an approved IDE or all controlled clinical trials have been completed.
- The clinical trial sponsor is actively pursuing marketing approval of the device.

CONTINUED ACCESS

The FDA may allow continued enrollment of subjects after a controlled clinical trial under an IDE has been completed in order to allow access to the Investigational Device while the marketing application is being prepared by the trial sponsor or is being reviewed by the FDA. There must a public health need or preliminary evidence that the device will be effective and there are no significant safety concerns.

EMERGENCY USE

An Investigational Device may be used to treat a patient with a serious or life-threatening disease or condition when there is no available alternative and insufficient time to submit to the FDA. In order to use an unapproved device in an emergency situation, the treating physician must determine that the patient meets

the above criteria and that there is potential benefit to the patient from the use of the unapproved device. The physician should obtain the following patient protection measures prior to initiating treatment:

- Informed consent from the patient or Legally Authorized Representative;
- Institutional clearance;
- IRB review and approval;
- An independent assessment from an uninvolved physician; and
- Authorization from the device manufacturer.

The FDA must be notified of the emergency use within 5 working days with a follow-up report that includes a summary of the conditions constituting the emergency, the patient protection measures followed, and the patient outcome. [21 CFR 812.35(a)(2)]

14.7 HUMANITARIAN USE DEVICES (HUD)

In accordance with [21 CFR 814.124], treatment with a HUD is subject to IRB Full Board initial and continuing review by the IRB. At the time of review, the IRB will determine if written consent from subjects for use of the HUD is necessary. If a physician in an emergency situation determines that IRB approval cannot be obtained in time to prevent serious harm or death to a patient, a HUD may be administered without prior IRB approval. In this instance, approval must be obtained from the Chief of Staff (or designee) of the applicable NYU Langone Hospital, and the Principal Investigator is required to provide written notification of the use to the IRB within five (5) days after use of the device.

The IRB requires that such written notification includes identification (specification without identifiers) of the subject, the date on which the device was used, and the reason for the use. It is the responsibility of the Principal Investigator to notify the FDA if the IRB withdraws approval for use of a HUD. The FDA should be notified within five (5) working days of notification of the withdrawal of approval. Principal Investigators are reminded that Humanitarian Use Device Exemptions are for clinical use only and HUDs can be used only for purposes outlined in the approved IRB application. Required medical device reports submitted to the FDA must be copied to the IRB. Post-approval requirements are detailed in [21 CFR 814.126].

15. QUALITY IMPROVEMENT & ASSURANCE (QIA) POLICY AND PROCEDURES

The Quality Improvement & Assurance division ("QIA Division") is a unit of NYU Langone Health's HRP and reports into the Senior Director of HRP. The QIA Division is charged with implementing a program of review of human research conducted at or on behalf of NYU Langone Health and its affiliates, and conducting internal audits and review of such research. This program of post-Institutional Review Board approval oversight also serves to promote continuing education for research personnel, and to support operational awareness and quality improvement for all components of the HRP at NYU Langone Health.

NYU Langone Health's HRP staff may conduct internal reviews, investigations and audits of ongoing Human Subjects Research in the following instances: (1) when the IRB directs an audit be conducted, (2) when a complaint or allegation of non-compliance is received, and/or (3) "not for cause" reviews of research (i.e., Routine Reviews). For a detailed discussion of investigations and audits, see: Section 12: Complaints, Non-Compliance, and Suspension or Termination of IRB approval of Research.

Policy Purpose

This policy establishes the program of internal compliance review of Human Subjects Research conducted by or under the auspices of NYU Langone Health. The compliance review process involves verifying subject eligibility, protocol adherence, and regulatory compliance. This internal program of reviewing clinical research serves to ensure that Human Subjects Research is conducted in compliance with federal, State, and local regulations, ICH Good Clinical Practice, and other NYU Langone Health policies. Its goal is to promote continuous improvement opportunities by providing education and greater awareness to researchers and staff of best practices and NYU Langone Health policies in order to ensure the conduct of consistently high quality research.

15.1 DEFINITIONS

CRF means a case report form - a printed, optical, or electronic document designed to record all of the protocol-required information to be reported to the sponsor on each trial subject.

QAR means a Quality Assurance Report, which is a report that summarizes non-compliance findings of the QIA Division's Directed Audit/Routine Review, following a standard QAR template.

CAPA means a Corrective Action and Prevention plan, which is a plan to document a summary of findings and key areas of regulatory non-compliance for a study and defines the necessary corrective actions to bring the study/studies back into compliance and prevent such identified non-compliance going forward.

DIRECTED AUDIT means an internal audit that is directed due to a concern about potential or actual research compliance issue. A Directed Audit may be directed by the IRB, the Office of Internal Audit, Compliance, and Enterprise Risk Management, the Office of General Counsel, or the Institutional Official for Human Research Protections.

EMA means the European Medicines Agency.

ESSENTIAL DOCUMENTS means documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.

FDA means the United States Food and Drug Administration.

GCP means Good Clinical Practice, which refers to an international standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights and confidentiality of trial subjects are protected.

HUMAN SUBJECTS RESEARCH means, for the purposes of this policy, any activity that either is "research" and involves "human subjects" as those terms are defined by DHHS regulations (45 CFR 46.102); or is a "clinical investigation" and involves "human subjects" as those terms are defined by FDA regulations (21 CFR 50 and 21 CFR 56).

IDE means investigational device exemption.

IND means investigational new drug.

NIH means the National Institutes of Health.

OHRP means the Office for Human Research Protections.

PRINCIPAL INVESTIGATOR means, for purposes of this policy, an individual who actually conducts research involving human subjects. In the event an investigation is conducted by a team of individuals, the Principal Investigator is the responsible leader of the team. In studies regulated by the FDA), this individual is referred to as the "Investigator" (i.e., under whose immediate direction a drug or test article is administered or dispensed to a subject).

ROUTINE REVIEW for purposes of this policy, means a comprehensive review of research activity conducted as part of the program of ongoing post-IRB approval, internal monitoring by the QIA Division. Routine Reviews are collaborative mechanisms between HRP's QIA Division staff, the Principal Investigator, and the research team. The purpose of a Routine Review is to provide assurance of the conduct and integrity of human research, improve human research protection, and identify quality improvement opportunities.

SOURCE DATA means all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source Data are contained in source documents (original records or certified copies).

SOURCE DOCUMENTS refers to original documents and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in a clinical trial).

SPONSOR for purposes of this policy, means an entity or person who takes responsibility for and initiates a clinical investigation. The Sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization. The Sponsor does not actually conduct the investigation unless the Sponsor is a Sponsor-Investigator (as defined below).

SPONSOR-INVESTIGATOR refers to an individual who both initiates and conducts an investigation. In FDA-regulated studies, the Sponsor-Investigator is the individual under whose immediate direction an investigational drug or test article is administered or dispensed to a subject. The term does not include any person other than an individual. The requirements of a Sponsor-Investigator include both those applicable to a Principal Investigator and a Sponsor.

15.2 POLICY

The QIA Division is authorized to schedule and conduct Routine Reviews and Directed Audits under this policy. Research personnel, including Principal Investigators, are expected to fully cooperate with all Routine Reviews and Directed Audits, and with inquiries based on allegations of non-compliance that are conducted by the QIA Division staff (internal audits), regulatory agencies, funding agencies, or study Sponsors (external audits), including taking appropriate steps to make necessary improvements to align their conduct of research with applicable federal regulations, state laws, and institutional policies.

ROUTINE REVIEWS AND SELECTION

TYPE OF ROUTINE REVIEWS

Routine Reviews are conducted on a scheduled basis by QIA Division Specialists and may also be conducted upon request by Principal Investigators. There are two types of Routine Reviews: Full Scope Review and Post-Approval Self-Assessment Review.

Full Scope Review
Full Scope Review is a comprehensive review conducted by a QIA Division Specialist of all research study activity under a specific protocol at one or more research locations. The review may be conducted in-person or remotely. A Full Scope Review assesses whether compliance standards have been met in 8 categories:

- Study enrollment status
- Execution of Informed Consent/Assents
- Maintaining Privacy/Confidentiality
- Participant Eligibility
- Documentation of Interventions/Observations & Study Procedures
- Safety Monitoring/Adverse Events
- Regulatory Documentation/Multisite Study Management
- Required Research Education/Institution Training

For Full Scope Reviews, the QIA Division Specialist will identify any findings or areas of concern and communicate them in a QAR. A draft of the QAR is sent to the Principal Investigator for review and comments. The Principal Investigator is invited to discuss the preliminary findings and suggestions for corrective action at an exit interview. Depending on the findings, the QIA Division may require corrective and preventive actions, including a time line for completion.

Post-Approval Self-Assessment Review
The QIA Division Specialist will send the Principal Investigator and/or delegated study staff an electronic request via Redcap link to the post-approval self-assessment form. This is an electronic tool created to improve overall site regulatory compliance in a pro-active manner. The self-assessment form will also serve as a way to educate investigators and research staff on what is expected of them in terms of regulatory documentation, IRB documentation, subject recruitment procedures, informed consent process, subject selection criteria, adverse event reporting, drug/device dispensing accountability, and case report form source documentation.

The QIA Division Specialist will review the completed form in Redcap and identify any findings or areas of concern. Depending on this review, the QIA Division will require corrective and preventive actions or a Full Scope Review by the QIA Division.

SELECTION CRITERIA FOR ROUTINE REVIEW

1. Studies will be selected for Routine Review by the Assistant Director of the QIA Division (or designees) at the discretion of and based on criteria established by the QIA Division.

2. Selection of studies for Full Scope Review will be random and based on study enrollment status, study characteristics such as study phase and risks, inclusion of vulnerable populations, rapid or high enrollment, new investigator or research coordinator, unlicensed investigator conducting an interventional study, multisite coordination responsibility, where privacy/confidentiality protection may be of concern, and other factors.

3. Studies may be selected for Post-Approval Self-Assessment review at random. For example, non-exempt studies may be selected for periodic self-assessment.

4. Additionally, Routine Review will be conducted on <u>all</u> studies with the following attributes:

- Studies conducted under an Investigator-held IND application or IDE application. Routine Review will occur after the enrollment of the first two subjects or as determined necessary by the IRB or Assistant Director of the QIA Division.

- Studies requiring an IRB continuing review cycle less than 1 year.
- Before scheduled inspections from government regulatory agencies (e.g., FDA, NIH, OHRP, EMA), whenever feasible.

DIRECTED AUDITS AND SELECTION

Directed Audits (also referred to as "For Cause") are generally initiated based on a concern, complaint, or an allegation of non-compliance and are used to inform decisions about the conduct of human subjects research and/or human subjects protection.

Studies may be selected for Directed Audit at the request of the IRB, the Institutional Official, Senior Director of HRP, the Office of Internal Audit, Compliance, and Enterprise Risk Management ("IACERM"), or the Office of General Counsel to obtain or verify information necessary to ensure compliance with regulations and institutional requirements.

FOLLOW-UP ASSESSMENTS AND AUDITS

Follow-up assessments and/or re-audits may be directed by the Assistant Director of the QIA Division or the IRB to confirm appropriate implementation of, and adherence to, the CAPA plan.

NOTIFICATION

Prior to initiating a Directed Audit or Routine Review, the Principal Investigator, and as appropriate, lead study coordinator, will be informed of the intention to conduct a review or audit and will be provided with the planned scope of review. For Directed Audits, the applicable department chair and (as applicable) vice-chair for research, division director, the Senior Director of HRP, Associate Director of NYU Langone Health IRB Operations, and Assistant Director of the QIA Division will be copied on the above communication to the Principal Investigator.

For Directed Audits only, the department chair and (if applicable) vice-chair for research and/or division director will be invited to have a pre-audit discussion with the Assistant Director of the QIA Division.

PREPARING FOR A DIRECTED AUDIT OR ROUTINE REVIEW

Prior to the Directed Audit or Routine Review, the Principal Investigator and study team are responsible for gathering and organizing all records in preparation for the review. It is expected that the QIA Division Specialists will have access to all required documents and the information be organized in such a way as to be easily located and identified. The Principal Investigator and study team must plan to have records available to the QIA Division Specialist(s) at the designated review location. If the QIA Division Specialist is expected to review electronic documents, it is the responsibility of the Principal Investigator and study team to ensure that appropriate access is available throughout the review process.

SCOPE AND PROCESS

ROUTINE REVIEWS

Documents Reviewed

The QIA Specialist will randomly select study documents on the following areas:

- Regulatory documents (paper or electronic binders): Approved study documents, IRB approval, RNIs, clinical laboratory certification and normal values, FDA correspondence and documents, IND/IDE correspondence and documents, etc.

- Informed Consent Forms (ICF) (Not less than 10 signed ICFs per study reviewed): Signed ICF and documentation of the consenting process.
- Participants' research records (enrolled subjects only; i.e., no screen failures). The number of subjects selected may vary depending on the type and complexity of the protocol and on the number of subjects enrolled. Source Documents and Case Report Forms (CRFs) from 1 or 2 study visits will be reviewed for accuracy and completion. In addition, study enrollment status, complete eligibility, AE, SAEs, and randomization records (if applicable) will be included in the review.
- Safety Monitoring: monitoring, tracking, and reporting of participant safety.
- IND/IDE folder (only when PI is the IND/IDE holder): application, annual submission, sponsor correspondence, FDA documents, etc.
- Multisite Study Management (only when NYU Langone Health PI is the lead investigator): maintenance of essential regulatory documentation at the local site or multisite level.
- Pharmacy/device files (if applicable): temperature log, investigational product and/or device accountability records.
- Staff files: Most updated CITI, most updated research financial diclosures, professional license (NYS professional license, DEA license if applicable), curriculum vitae, and any other specific study training.

Expanding Scope of Routine Review

The scope of a Routine Review (number of studies, types of documents reviewed) may be expanded during the course of the review at the discretion of the Assistant Director of the QIA Division based on ongoing findings in the course of Routine Review.

ROUTINE REVIEW OF STUDIES CONDUCTED UNDER AN INVESTIGATOR-HELD IND APPLICATION OR IDE

A faculty IND/IDE sponsor audit is aimed at confirming compliance with FDA IND and IDE sponsor responsibilities. Review of Sponsor records will focus on:

- IND or IDE application
- Sponsor Regulatory Master File
- Drug Master File (as applicable)
- Study site selection and qualification (as applicable)
- Annual IND Safety update reports to the FDA
- Expedited IND Safety reporting to the FDA, and research sites
- Sponsor medical monitoring
- Sponsor site monitoring (as applicable)
- Study data management.

DIRECTED AUDITS

The scope of Directed Audits will depend on the nature of the underlying concern, complaint, or allegation.

REVIEW AND AUDIT FINDINGS

CONCLUDING A ROUTINE REVIEW OR DIRECTED AUDIT

At the conclusion of a Routine Review or Directed Audit, preliminary findings will be shared with the Principal Investigator and study team (as applicable) at an exit meeting.

The IRB will not be notified of results from the results of a Routine Review, unless the results of the review reveal significant deficiencies in the protection of human subjects in research, or if the results indicate subjects are at risk of harm.

In the case of Directed Audits, findings are confidential peer review information and do not become part of the study record. However, upon completion of a Directed Audit, the findings may be reported to the IRB and applicable IRB Chair.

GRADING OF FINDINGS

Findings will be graded by QIA according to the following classifications.

Critical
Conditions, practices, or processes that adversely affect the rights, safety or well-being of the subjects and/or violated applicable regulations or NYU Langone Health HRP policies and/or significantly impacted the quality and integrity of data and require prompt reporting to the IRB by the Principal Investigator. Examples: pattern of deviations classified as major; bad quality of the data; and/or absence of source documents. Manipulation and intentional misrepresentation of data also belong to this group.

Major
Conditions, practices, or processes that might adversely affect the rights, safety or well-being of the subjects and/or violate applicable regulations or NYU Langone Health HRP policies and/or has potential to significantly impact the quality and integrity of data. Findings in this category, may require the Principal Investigator to report to the IRB as soon as possible. Findings classified as Major are serious findings that clearly violate applicable regulations or NYU Langone Health HRP Policies. Examples: pattern of deviations and/or numerous minor observations.

Minor
Conditions, practices, or processes that would not be expected to adversely affect the rights, safety, or well-being of the subjects and/or violate applicable regulations or NYU Langone Health HRP policies and/or did not significantly impact the quality and integrity of data. Note: Many minor observations may in sum be deemed equivalent to a Major finding.

QUALITY ASSURANCE REPORT (QAR)

A QAR will be generated by QIA Division staff and reviewed by the QIA Assistant Director. The QAR will then be e-mailed to the Principal Investigator and lead study coordinator. For Directed Audits, the applicable department chair, division director, and vice-chair for research (if applicable), Senior Director of HRP, Director of NYU Langone Health IRB Operations, Assistant Director of the QIA Division, and the IO will be copied on the email.

RESPONSE TO FINDINGS

If appropriate, the QIA Division will provide a recommended CAPA plan template to the Principal Investigator. The Principal Investigator should use the template as the basis for creating their own CAPA plan for submission to the QIA Division for review and approval and IRB as needed. If the IRB determines that the CAPA plan submitted by the Principal Investigator is inadequate, the IRB may add to or impose its own CAPA plan. Principal Investigators are required to reply to the QIA Division to attest to their having read and

understood the plan and its requirements. The CAPA plan will be shared with the applicable department chair and vice-chair for research or division director (if applicable), and the IO, as appropriate.

DEPARTMENTAL/DIVISIONAL REPORTING

Annual reports of aggregate data on Routine Reviews and Directed Audits (not linked to any specific protocols/Principal Investigators) will be generated and shared with the Senior Director of HRP and IRB Chair. The Assistant Director of the QIA Division will provide a report of general trends and findings to department and division chairs on an as-needed basis.

DELEGATION OF RESPONSIBILITY

1. The QIA Division may delegate aspects of its program to entities within NYU Langone Health that have adequate resources and expertise to conduct Routine Reviews, as determined by the QIA Division. Any such entity is referred to as a local compliance office ("LCO"). The QIA Division may also delegate auditing responsibility to external entities subcontracted by the QIA Division.

2. The details of the delegation of responsibility to provide Routine Review services must be documented in a Letter of Agreement between the QIA Division and the applicable LCO or non-NYU Langone Health subcontractor. LCOs and subcontractors must provide copies of review findings to the QIA Division. The Letter of Agreement shall be signed by the Senior Director of HRP and the Director of the LCO or authorized party on behalf of the subcontractor.

3. The QIA Division will re-assess LCOs and subcontractors on a regular basis, or at least every 3 years, to confirm compliance with their delegated responsibilities as noted in the Letter of Agreement.

4. The Assistant Director of the QIA Division may rescind a Letter of Agreement delegating responsibility to provide an oversight function if the LCO or subcontractor is found to have inadequate expertise or resources to provide the delegated responsibilities, or is in serious or continued noncompliance with the requirements of the Letter of Agreement, or at the discretion of the IO.

COMPLIANCE REVIEW RECORDS

1. All QAR and/or audit reports, CAPA, IRB correspondence and federal notifications will be maintained by the QIA Division.

2. Researchers should maintain their QARs and CAPAs separately from their study regulatory records. All records related to the study must be maintained for the duration specified in NYU Langone Health's *Policy on Retention of and Access to Research Data*.

AUDIT OF RESEARCH PROJECTS BY EXTERNAL ENTITIES

Studies may also be audited or inspected by external entities, such as a regulatory body or study Sponsor. The Principal Investigator (or designee) must immediately inform the relevant individuals/offices within NYU Langone Health upon notification by the external entity of an upcoming audit or inspection. This requirement does not apply to routine monitoring visits conducted by a Sponsor or contract research organization. For more information on NYU Langone Health individuals and offices that must be notified, see SOP #HSR-401, *Audits of Research Projects by External Entities*.

QUESTIONS

Any questions relating to this policy should be directed to the Assistant Director of the Quality Improvement & Assurance Division.

POLICY ENFORCEMENT

Violations of this policy are subject to disciplinary action, up to and including termination of employment or association with NYU Langone Health, in accordance with NYU Langone Health disciplinary policies and procedures applicable to the individual in question.

In addition, if a Principal Investigator and research team does not cooperate with the QIA Division's efforts to schedule or conduct a Routine Review or Directed Audit, the QIA Division may report non-compliance to the Senior Director of HRP (and the IO, if necessary) who may suggest a Directed Audit or expansion of the scope of Routine Review.

16. PRINCIPAL INVESTIGATOR RESPONSIBILITIES

Principal Investigators are ultimately responsible for the conduct of research. Although they may delegate certain responsibilities in the research, the Principal Investigator must maintain oversight and retains ultimate responsibility for the conduct of those to whom they delegate responsibility.

In order to satisfy the requirements of this Policy, Principal Investigators who conduct research involving human subjects at or under the auspices of NYU Langone Health must:

- develop and conduct research that is in accordance with the ethical principals in the *Belmont Report;*
- develop a research plan that is scientifically sound and minimizes risk to the subjects;
- have sufficient resources necessary to protect the human subjects, including:
    - access to a population that would allow recruitment of the required number of subjects
    - sufficient time to conduct and complete the research
    - adequate numbers of qualified research staff
    - adequate facilities
    - a process to ensure that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions
    - availability of medical or psychological resources that subjects might require as a consequence of the research;
- ensure that all study-required procedures in a study are performed with the appropriate level of supervision and only by individuals who are licensed or otherwise qualified to perform such under the laws of the State of New York and the NYU Langone Health policies;
- ensure that all key study personnel are educated in the regulatory requirements regarding the conduct of research and the ethical principles upon which they are based;
- protect the rights and welfare of prospective subjects;
- ensure that risks to subjects are minimized by:
    - using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
    - whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes;
- recruit subjects in a fair and equitable manner;
- have plans in place to monitor the data collected for the safety of research subjects, as applicable;
- protect the privacy of subjects and maintain the confidentiality of data;
- when some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, include additional safeguards in the study to protect the rights and welfare of these subjects;
- have a procedure to receive complaints or requests for additional information from subjects and respond appropriately;

- ensure that pertinent laws, regulations, and institution procedures and guidelines are observed by participating co-investigators and research staff;
- obtain and document informed consent as required by the IRB and ensure that no human subject is involved in the research prior to obtaining their consent on an up-to-date IRB-approved consent form;
- ensure that all research involving human subjects receives IRB review and approval in writing before commencement of the research;
- comply with all IRB decisions, conditions, and requirements;
- ensure that protocols receive timely continuing IRB review and approval;
- report problems that require prompt reporting to the IRB (*see*: Required Reports to the IRB);
- obtain IRB review and approval in writing before changes (i.e. amendments) are made to approved protocols or consent forms; and
- seek IRB assistance when in doubt about whether proposed research requires IRB review.

16.1 INVESTIGATOR CLASSIFICATIONS: WHO MAY SERVE AS PRINCIPAL INVESTIGATOR FOR NYU LANGONE HEALTH HUMAN SUBJECTS RESARCH

PRINCIPAL INVESTIGATORS

The NYU Langone Health IRB recognizes one Principal Investigator for each study. The Principal Investigator has oversight responsibility for the research activities covered under his/her research protocol.

At NYU Langone Health, only faculty or staff members with a NYUGSoM or NYU LISoM-paid appointment may serve as the Principal Investigator or as the faculty sponsor on a research project involving human subjects. Individuals whose primary appointment is as a non-compensated NYUGSoM or NYU LISoM faculty member cannot serve as Principal Investigator or faculty sponsor without the express approval of the applicable department chair.

Any investigator whose status is considered to be "in training" (i.e. students and medical residents) may not serve as Principal Investigator, but may serve as a co-Investigator (Co-I).

All dental residents in NYU Langone Hospitals dental residency programs who are in training at locations outside of NYU Langone Health may serve as Principal Investigator for Minimal Risk studies, but only if an eligible, qualified mentor is listed as a co-investigator.

NYU Meyers College of Nursing nurses holding doctorate-level degrees (e.g, DNP, PhD, DNS, DPH, EdD) may serve as a Principal Investigator. Any NYU Langone Health nurse may serve as a Principal Investigator, but only if an eligible NYU Langone Health nurse with a doctorate-level degree (e.g., DNP-Ph.D., DNS, DPH, EdD) is listed as a co-investigator.

Studies that will be conducted by nurses are required to be submitted to the NYU Langone Health Departments of Nursing - Center for Innovations in the Advancement of Care (CIAC) for a review of the protocol and for assistance in obtaining clearance to serve as a Principal Investigator.

All dental residents in NYU Langone Hospitals dental residency programs who are in training at locations outside of NYU Langone Health may serve as Principal Investigator for Minimal Risk studies, but only if an eligible, qualified mentor is listed as a co-investigator.

Protocols that require skills beyond those held by the Principal Investigator must be modified to meet the investigator's skills, or have one or more additional qualified faculty or staff listed as co-investigator.

STUDENT INVESTIGATORS

Other than as permitted above, students (including Fellows, Residents, medical students, dental students, nursing students, etc.) may not serve as Principal Investigator. They must have a faculty sponsor who meets the Principal Investigator eligibility criteria and who will serve as Principal Investigator and faculty advisor on the study.

16.2 PROTOCOL DEVELOPMENT

The Principal Investigator is responsible for determining whether a protocol constitutes human subjects research which requires IRB review and approval, and if so, for ensuring that the study protocol and related information are submitted in accordance with the IRB's policies and procedures, applicable regulations, and institutional policies.

DETERMINATION OF HUMAN SUBJECTS RESEARCH

When developing a protocol, the Principal Investigator or a member of the protocol research team may contact IRB Operations for a determination whether the proposed study constitutes human subjects research, and if so, what level of review would be required. Contact with IRB Operations may be in the form of a phone call, by letter, or by email and must include a brief description of the proposed research. IRB Operations will respond to the Principal Investigator or member of the research team by phone, letter, or email.

PRE-IRB DEPARTMENTAL REVIEW

In the event the Principal Investigator's department (or department that is administering the proposed research) has a feasibility and/or scientific review process in place, the Principal Investigator is responsible for ensuring that the research protocol is reviewed by the approved department reviewer, if applicable. The Principal Investigator must make any changes to the protocol that are recommended by the department reviewer or committee. The intent of this Policy is to ensure that any issues that have been identified as needing to be addressed prior to review by the full IRB are fully addressed, thus avoiding delays in receiving IRB approval for the research study.

Following departmental review and sign-off by Department Chairs or other appropriate institutional official(s), the Principal Investigator must submit the required materials to IRB Operations.

SUBMISSION REQUIREMENTS

Principal Investigators must provide complete answers to all questions on the IRB/Research Navigator application for new protocol review and ensure that information in the consent form is consistent with the research plan.

The proposed consent and/or assent form (if applicable) must include or address:

- the general principles and basic elements of informed consent;
- translated consent documents, as necessary, considering likely subject population(s);
- NYU Langone Health IRB-approved formats for consent forms and assent forms; and
- waiver of consent conditions.

The Principal Investigator must ensure that the protocol and attachments are submitted to other institutional regulatory committee offices (e.g., Institutional Biosafety Committee, Radiation Safety Committee) as applicable for review and approval.

If the research is DHHS-sponsored, the materials submitted to the IRB reviewer must include the entire sponsoring application. If there is a significant variation between the DHHS application and the IRB protocol, it is the Principal Investigator's responsibility to identify and justify the discordance.

If the research is FDA-regulated and industry-sponsored, the IRB submission must include the complete sponsor's protocol as well as, for drug studies, the investigator's brochure [21 CFR 312.23(a)(5) and 312.55], and FDA form 1572.

16.3 CHANGES TO IRB-APPROVED RESEARCH

Principal Investigators must seek IRB approval before making any changes in approved research, even if the changes are planned for the period for which IRB approval has already been given. The only exception to this is if the change is necessary to eliminate an immediate hazard to a subject, in which case the IRB must then be notified at once.

Minor protocol changes (i.e., changes that do not involve increased risk or discomfort to subjects) may be authorized by the IRB Chair or his/her designee. A completed Application for Approval of an Amendment, located on the HRP's website, with information specifying the changes requested, a revised consent form (if applicable), and a copy of the approved protocol with the proposed changes highlighted, should be sent directly to IRB Operations according to IRB Operations procedures. The IRB Chair or Senior Director, HRP must sign and return a letter to indicate approval of the minor protocol changes. IRB-approved amendments to ongoing research do not serve to extend the term of the IRB approval/expiration date. For further information regarding amendments, see: Modification of an Approved Protocol.

16.4 CONTINUING REVIEW AFTER PROTOCOL APPROVAL

Ongoing research studies must be reviewed by the IRB at least annually, or more often, if the IRB finds that the degree of risk to subjects warrants more frequent review. This review must take place prior to the end of the approval period noted on the approved protocol; otherwise, subject recruitment/enrollment must be suspended and, if the research is DHHS-sponsored, the sponsoring agency must be notified.

It is the responsibility of the Principal Investigator to submit a timely continuing review application. The Principal Investigator should allow sufficient time for development and review of renewal submissions. Note: The "approval date" and the "approval expiration date" are listed on all IRB certifications. By federal regulation, no extension to that date can be granted.

Principal Investigators must provide complete answers to all questions on the IRB application for continuation (*Request for Continuation* form), the current consent document and newly proposed consent document. Note: Additional information may be required as specified in the original protocol review. For further information regarding continuing review, see Continuing Review of Active Protocols.

16.5 REQUIRED REPORTS TO THE IRB

PROGRESS REPORTS

It is the responsibility of the Principal Investigator to report the progress of the research to the IRB in the manner and frequency prescribed by the IRB, but no less than once a year.

When an approved study is completed, the Principal Investigator must promptly notify the IRB and file with the IRB a final study progress report.

Once data collection has been completed and the study is closed at NYU Langone Health and/or other study sites, a final study closure submission must be made to the IRB. Once this final submission is complete, the Principal Investigator is not required to submit any further reports of the study to the IRB.

REPORTABLE NEW INFORMATION

Principal Investigators must report reportable new information including but not limited to complaints, non-compliance, and protocol deviations to IRB Operations in accordance with Section 8.8: Reportable New Information

The following Section 16.6: Protocol Exceptions and Deviations further describes how protocol exceptions must be reported to the IRB.

16.6 PROTOCOL EXCEPTIONS AND DEVIATIONS

PROTOCOL EXCEPTIONS

Protocol exceptions are defined as circumstances in which the specific procedures called for in a protocol are not in the best interests of a specific patient/subject (Example: patient/subject is allergic to one of the medications provided as supportive care). Usually a protocol exception is a violation that is anticipated and happens with prior agreement from the study sponsor.

Protocol exceptions must be approved by the study sponsor and IRB before being implemented.

Protocol exceptions may not increase risk or decrease benefit, affect the subject's rights, safety, welfare, or affects the integrity of the resultant data.

PROTOCOL DEVIATIONS

A **protocol deviation** is defined as a violation that is unanticipated and happens without any prior agreement (Examples: protocol visit scheduled outside protocol window, blood work drawn outside protocol window, etc.). The IRB will review these reports for frequency and may audit any protocol in which frequent deviations occur. Repeated protocol deviations may be ruled by the IRB to constitute non-compliance resulting in suspension of IRB approval.

It is the responsibility of the Principal Investigator not to deviate from the protocol approved by the IRB, except to avoid an immediate hazard to the subject. The Principal Investigator must submit an amendment request to the IRB and receive written approval prior to implementation of any change to the protocol.

Deviations that increase risk have potential to recur or undertaken to eliminate an immediate hazard would be considered an Section 8.8: Reportable New Information.

When a study sponsor requests that the IRB be notified of a protocol deviation, the Principal Investigator is responsible for ensuring that the completed *Protocol Deviation/Exception* form is forwarded to the IRB Chair or designee for review.

PROTOCOL EXCEPTIONS REPORTING AND REVIEW

A *Protocol Exception Appendix* must be submitted with a *Reportable New Event* form for those events that qualify as a protocol exception. These reports should be filed with IRB Operations.

- IRB Operations will forward the report to the IRB Chair or designee for review and signature.

- The IRB Chair may choose to either approve the protocol exception if they find the event does not increase risk of harm or decrease benefit to the subject, or may refer the protocol exception to the next convened IRB meeting for discussion. The Principal Investigator may be asked to appear at that meeting to answer any questions or clarify issues for the IRB.

16.7 PRINCIPAL INVESTIGATOR-REQUIRED RECORD KEEPING

Principal Investigators must retain copies of approved IRB documents and correspondence with the IRB in the applicable study record, and must implement a system to comply with approval expiration dates.

In addition to providing a copy of the signed and dated consent form to each subject, a copy of the signed consent form must be retained securely by the Principal Investigator in the research record for a minimum of five (5) years after completion of the research.

The Principal Investigator will further maintain the following in the research record, each as applicable:

(1) current curriculum vitae (CV);
(2) study protocol/investigational plan;
(3) records of receipt and disposition of study drugs;
(4) records of receipt and disposition of study devices;
(5) list of any co-investigators with their curriculum vitae;
(6) certification that all physicians, dentists, and/or nurses performing study procedures have appropriate valid licenses for the duration of the study;
(7) records of animal study reports that relate to the proposed human subject research;
(8) case histories with particular documentation on evidence of Investigational Drug and/or Investigational Device effects. Emphasis is on safety, toxicity and possible untoward happenings. All unexpected adverse drug or device effects are reportable; even if the Principal Investigator considers that the event is not related to the drug or device. All unexpected Adverse Events must be reported immediately to the IRB in the manner defined by the protocol;(8) IRB letters of approval and ethics committee approval letters (if applicable); and
(9) documentation of Investigational Device training.

16.8 TRAINING AND ONGOING EDUCATION OF PRINCIPAL INVESTIGATOR AND RESEARCH TEAM

A component of a comprehensive human research protections program is an education program for all individuals involved with human research subjects. NYU Langone Health is committed to providing training and an on-going educational process for Principal Investigators and members of their research teams related to ethical concerns and regulatory and institutional requirements for the protection of human subjects. The Principal Investigator should ensure that he or she is trained, and ensure that members of his or her research team receive training and education necessary to correctly perform their delegated responsibilities.

This Policy establishes NYU Langone Health's requirements for training and ongoing education of Principal Investigators and Research Team members for conduct of human subjects research. This Policy does not impact any requirements of study sponsors, and any sponsor-required training in human subjects research or Good Clinical Practice.

ORIENTATION

All Principal Investigators and members of their Research Team (also known as "Key Personnel") must review core training documents provided by NYU Langone Health, including the *NYU Langone Health IRB and Human Subjects Research Protections Policies & Procedures*, and the "*Belmont Report: Ethical Principals and Guidelines for the Protection of Human Subjects of Research*".

INITIAL EDUCATION

All Principal Investigators and members of their Research Teams must complete initial CITI training. There is no exception to this requirement. The Principal Investigator and Key Personnel must complete one of the basic courses offered through the CITI web-based program. While several basic course modules are available, Principal Investigators are responsible for completing the course relevant to the research activities being conducted and must ensure that each of their Key Personnel complete such courses prior to conducting human subjects research. Basic course options in CITI include: Biomedical, Social Behavioral, Research with Data or Laboratory—Specimens–Only, and Students Conducting No More Than Minimal Risk Research.

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

While research protocols and applications for continuing review will be accepted and reviewed regardless of required training completion, neither the Principal Investigator nor any member of the Research Team can carry out research-related activities until the CITI training requirement has been satisfied.

WAIVER OF INITIAL EDUCATION

If Principal Investigators or members of their Research Team can verify that they have successfully completed human subjects research training equivalent to that required by the NYU Langone Health IRBs, they may request a waiver of the requirement for initial education. However, all Principal Investigators or members of their Research Team must complete the institutional requirements of continuing education.

CONTINUING EDUCATION AND RECERTIFICATION

With the exception of faculty conducting research, Research Team members must complete CITI training every three (3) years after completion of their initial certification for as long as they are involved in human subjects research at NYU Langone Health. Research Team members who are faculty are required to complete the CITI training only once, prior to conducting human subject research unless they receive a waiver of the initial education requirement. These requirements apply to completion of appropriate refresher modules at the CITI web-based training site. Faculty members are not required to complete refresher modules after their initial CITI training, but are encouraged to do as needed.

While research protocols and applications for continuing review will be accepted and reviewed regardless of required training completion, neither the Principal Investigator nor any member of the Research Team can carry out research-related activities until the CITI training requirement has been satisfied.

Investigators and members of Research Teams who also serve as IRB Chair, IRB committee members, or IRB Operations staff must satisfy the training requirements for IRB committee members and IRB Operations staff described in this Policy under Training & Ongoing Education of Chair and IRB Members in Regulations, Procedures.

Questions about CITI requirements for human subjects research may be directed to irb-education@nyulangone.org.

ADDITIONAL RESOURCES

Human research protection information will be made available on the NYUGSoM IRB websites on an ongoing basis to ensure that the NYU Langone Health research community is apprised of current regulatory and policy requirements and training opportunities.

16.9 CONFLICT OF INTEREST

This Policy and procedures apply to both Financial Interests related to human subjects research and Non-Financial Conflicts of Interest (both defined below) and are guided by Code of Federal Regulations [Title 42 of the Code of Federal Regulations (CFR) Part 50 Subpart F] that promotes objectivity in research to ensure conflict of interests do not adversely affect the protection of subjects or the credibility of the NYU Langone Health Human Research Protections, including its NYU Langone Health IRBs.
For clinical studies involving the use of new human drugs and biological products or medical devices, certifications and disclosure requirements are defined in FDA regulations, 21 CFR Part 54.

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

It is the policy of the NYU Langone Health IRB to preserve public trust in the integrity and quality of research at the organization by minimizing actual or perceived conflict of interest in the conduct of research. Under NYU Langone Health's *Policy on Conflicts of Interest in Research and Other Sponsored Programs* (the "Conflicts of Interest in Research Policy") and its *Policy on Institutional Conflicts of Interest in Human Subjects Research* (the "Institutional Conflicts Policy"), NYU Langone Health and all of its investigators including Research Team members participating in research at NYU Langone Health have a primary obligation to conduct the research free of the appearance of conflict. Participating in research that might be perceived to be compromised due to a personal or institutional interest is contrary to this commitment, unless the conflict of interest is managed or eliminated. Under certain circumstances, an investigator's personal interest (or NYU Langone Health's institutional interest) might be too significant to permit participation in the research. The *Conflicts of Interest in Research Policy* and the *Institutional Conflicts Policy* accommodate current federal regulations designed to protect the integrity of federally funded research and all other applicable laws and regulations and are consistent, to the extent appropriate for the NYU Langone Health community with the latest best practices recommendations of the Association of American Medical Colleges.

The Principal Investigator and Research Team members must comply with conflict of interest policies of their institution/organization. If the institution does not have a conflict of interest policy, the terms of an applicable agreement (such as an IRB reliance agreement) apply.

DEFINITIONS

COMPELLING CIRCUMSTANCES means, for purposes of this Policy, facts that convince NYU Langone Health's Executive Vice President and Vice Dean for Science, Chief Scientific Officer and/or the CIMU that an Investigator and/or NYU Langone Health may participate in a research study despite a Significant Financial Interest or Institutional Financial Interest, as applicable. Factors that may be evaluated to determine whether Compelling Circumstances exist are listed in NYU Langone Health's *Procedures on Research Conflict of Interest and Sponsored Programs*.

CONSULTING COMPENSATION means, for purposes of this Policy, salary, consulting fees, honoraria, paid authorship, lecture fees, other emoluments, stocks, stock options, Royalty Income or "in-kind" compensation directly or indirectly received by an Investigator or the institution from an organization (or entitlement to the same), outside of the costs of conducting research, in the prior calendar year or are expected to be received in the current or next calendar year. Such items may be received in connection with a Management, Board, or Employment Position or for consulting, lecturing, or service on a scientific advisory board, data safety monitoring board, clinical trial steering committee or executive committee, or other committee for an outside entity.

CONFLICT OF INTEREST arises in a human subjects research study when NYU Langone Health's designated officials reasonably determine that an Investigator's or institution's (NYU's or NYU Langone Health's) Financial Interest could affect, or appear to affect, the design, review, conduct, results or reporting of the research.

FINANCIAL INTEREST for purposes of this Policy, is held when an Investigator participating in a research study or a member of his or her Immediate Family has a personal financial interest that reasonably appears to be related to the Investigator's responsibilities to NYU Langone Health and includes all personal financial interests in the research funding sponsor or any other financially-interested company, or (ii) has intellectual property rights that cover a product or process being tested in the research. Examples are as described in the *Policy on Conflicts of Interest in Research* and include: Management, Board, or Employment positions, Ownership Interests, Consulting Compensation, paid/reimbursed travel, Royalty Income, and Intellectual Property Rights.

IMMEDIATE FAMILY MEMBER refers to an individual's spouse, domestic partner, person in a civil union, or similar relationship, parent, dependent child, or other family members residing in the individual's household.

INSTITUTIONAL FINANCIAL INTEREST for purposes of this Policy, is held when either (i) NYU or NYU Langone Health receives or might reasonably be expected to receive Royalty Income from the sale of a product covered by any patent (whether issued or pending), copyright, license, or other intellectual property right, held by NYU or NYU Langone Health and proposed to be used in a human subjects research project; and/or (ii) NYU or NYU Langone Health holds or proposes to hold, directly or indirectly, any equity interests in any amount (or entitlement to the same) in the research sponsor through NYU's or NYU Langone Health's technology licensing activities or investments related to such activities with the research sponsor.

INTELLECTUAL PROPERTY RIGHT consistent with its definition in the *Policy on Conflicts of Interest in Research*, means an issued or pending patent, license, or copyright covering products or processes being used in a research project, and includes: the right to income from NYU in connection with a patent, license, or copyright held by or to be held by NYU.

INVESTIGATOR for the purpose of this Policy and consistent with the definition in NYU Langone Health's *Conflicts of Interest in Research* policy, means "any person in the NYU Langone Community, regardless of title or position, who is any of the following in connection with a" human subjects research study "at or under the auspices of NYU Langone Health" who is

- responsible for the design, conduct or reporting of the research;
- proposes to be the Principal Investigator/program director or key personnel in a grant application for the research that is submitted by NYU Langone Health;
- serving as the Principal Investigator/program director, co-investigator, sub-investigator, or key personnel on the research; or
- listed as an investigator or coordinator on the IRB application for the research.

NYU LANGONE COMMUNITY means NYU Langone Health faculty (including adjunct, clinical, voluntary, and visiting faculty); researchers, who may include persons participating in research at or under the auspices of NYU Langone Health; employees; professional staff, including medical, dental and nursing staff; volunteers; fellows; trainees and post-doctoral appointees; students; and consultants, vendors and contractors.

Under the *Conflicts of Interest in Research* policy, ***INVESTIGATOR*** also includes outside persons (e.g., sub-grantees, contractors, collaborators or consultants of NYU Langone Health) who are determined by NYU Langone Health, in consultation with the Principal Investigator/program director of the [study] to be responsible for the design, conduct, or reporting of the [study] conducted at or under the auspices of NYU Langone Health."

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

OWNERSHIP INTEREST means any equity interest, including stock and stock options in any amount in either a publicly-traded or non-publicly-traded entity, *except* those held in mutual funds, provided that the Investigator or any of his/her Immediate Family members do not have 15% or greater interest in the fund and do not have a Management, Board, or Employment position in the fund.

ROYALTY INCOME means payment linked to product sales, or the written contractual right to receive future royalty payments, directly or indirectly, under an issued or pending patent, license, or copyright, that has been received in the prior calendar year or is expected to be received in the current or next calendar year.

SIGNIFICANT FINANCIAL INTEREST, for the purpose of this Policy, is a Financial Interest that is

(a) any Management, Board or Employment Position (including as a director, trustee, partner, senior executive, officer or employee), regardless of compensation;

(b) Ownership Interests (including stocks, options, and warrants) related to the research, greater than $10,000 when aggregated for the Immediate Family;

(c) Ownership Interests of any amount in a privately-held company;

(d) Consulting Compensation, including salary, consulting income, and honoraria), paid/reimbursed Travel for personal benefit as determined by the CIMU (e.g., a gift or a trip whose primary purpose is pleasure or celebration), and Royalty Income, when aggregated, of more than $25,000 in any relevant year; or

(e) any Intellectual Property Right being tested, developed, or validated in the research.

INDIVIDUAL CONFLICTS ON INTEREST

An individual Conflict of Interest may exist whenever an Investigator has a Financial Interest related to research in which he/she participates, including any interest in entities sponsoring or otherwise affected by the research and any interests in products being used in the research. The *Conflicts of Interest in Research Policy* identifies requirements for disclosure, and procedures for evaluation and either management or elimination of potential Conflicts of Interest in research. Under the *Conflicts of Interest in Research Policy*, Investigators participating in research and other sponsored programs must disclose all Financial Interests that reasonably appear to be related to the Investigator's responsibilities at NYU Langone Health and the

specific research project. NYU Langone Health, through its Conflicts of Interest Management Unit ("CIMU"), a division of its Office of Internal Audit, Compliance and Enterprise Risk Management ("IACERM"), will then review and evaluate such disclosures, determine whether the Financial Interest could give rise to a Conflict of Interest in the research, and determine whether the Conflict of Interest can be managed or must be eliminated in order for the individual to engage in the research project.

- If the CIMU determines that the disclosed Financial Interest is not a Significant Financial Interest, the CIMU will determine if a Conflict of Interest exists. If so, the disclosing Investigator's participation in the research will normally be permitted, subject to the terms of a CIMU-issued conflict of management plan.

- If an Investigator discloses a Significant Financial Interest that could give rise to a Conflict of Interest, the CIMU will first (1) determine whether or not Compelling Circumstances exist to justify the Investigator's participation in the research, notwithstanding the Significant Financial Interest, and (2) if the matter gives rise to a significant potential Conflict of Interest, the CIMU will, with consultation from the Office of General Counsel and/or NYU Langone Health's Executive Vice President and Vice Dean for Science, Chief Scientific Officer, use diligent efforts to eliminate or manage the conflict. If the CIMU is not able to eliminate or manage the conflict, or if so recommended by the Executive Vice President and Vice Dean for Science, Chief Scientific Officer, the CIMU may refer the matter to NYU Langone Health's Business Conflict of Interest Committee ("BCOIC").

  If the CIMU determines Compelling Circumstances exist for the Investigator's participation in the research, the CIMU will approve a conflict management plan. In order for the Investigator to participate in the research, the conflict management plan must be agreed to by both the project's Principal Investigator and the Investigator (if different). If Compelling Circumstances are not found or the conflict management plan is not agreed-to, the Investigator may carry out the research only if the Conflict of Interest is eliminated.

To assure that all potential Conflicts of Interest are identified, the *Conflicts of Interest in Research Policy* requires all that Investigators participating in a research project (including Principal Investigator, co-investigators and other Research Team Members) submit, at the time the project is first submitted to the IRB to SPA or the IRB, protocol-specific disclosures of personal Financial Interests of the individual and his/her Immediate Family. In addition, all such individuals will be required to complete and return a disclosure form on an annual basis under which they disclose any Financial Interests related to their responsibilities at NYU Langone Health and its affiliates. The IRB or SPA will forward to the CIMU any project-specific disclosure in which an Investigator has indicated a Financial Interest for further review, evaluation, and determination of whether the Financial Interest could give rise to a Conflict of Interest in the research in accord with the *Conflicts of Interest in Research Policy*.

For any study where an Investigator or other Research Team member discloses a Financial Interest, the IRB will not issue its final initial approval of the study until the NYU Langone Health CIMU and/or the BCOIC has completed its review and evaluation of the potential conflict as required under the *Conflicts of Interest in Research Policy*. The reviewing IRB may not approve research protocols referred to the CIMU and/or the BCOIC that have not been approved by the CIMU and/or the BCOIC or approve monitoring procedures or other conditions that are less restrictive than those imposed by the CIMU and/or the BCOIC. Upon completion of its review and evaluation, the CIMU will notify the IRB of the final determination of the Conflict of Interest review and, if applicable, will submit to the IRB the conflict management plan issued by the CIMU or the BCOIC and approved by the applicable Investigator(s). Upon receipt, the IRB Chair (or designee) will review the conflict management plan and report the results of the evaluation and management plan to the convened IRB or the reviewer using the expedited procedure before issuing the IRB's final initial approval of the study. The IRB may modify the plan to impose more stringent restrictions than those imposed by the CIMU or the BCOIC in order to protect research subjects. IRB Operations must

document completion of the review required under the Conflicts of Interest in Research in the applicable IRB protocol/study file, which will include retaining a copy of the final, approved conflict management plan.

If an Investigator's Financial Interests in a research project change during the course of the study, the Investigator is required to submit a revised Investigator Financial Interest Disclosure Form to the IRB prior to acquiring such new Financial Interests. If there are material changes from the prior disclosures, the CIMU and the BCOIC will review the change to determine if the conflict management plan on file is adequate and appropriate for the changed circumstances.

In addition, every Investigator listed on the IRB protocol is required to submit a new disclosure form at the time of each annual continuing review of a research project. The IRB will review material changes to the disclosures as part of its continuing review process. Approvals of continuing review for the research will not be held in the event of a change to an Investigator's financial interest disclosure. However, if there is a modification to add new study personnel and the new study personnel discloses a Financial Interest, the IRB will hold its continuing review approval until the NYU Langone Health CIMU and/or the BCOIC has completed its review and evaluation of the potential conflict.

INSTITUTIONAL CONFLICTS OF INTEREST

The *Institutional Conflicts Policy* sets forth procedures for reporting, evaluation, and either management or elimination of potential institutional Conflict of Interests ("ICOIs") in research. Under the *Institutional Conflicts Policy*, all potential ICOIs require disclosure, evaluation and either management or elimination in order for the research to be conducted at or by NYU Langone Health. Under the *Institutional Conflicts Policy*, an ICOI "arises in human subjects research when a financial interest of NYU or NYU Langone Health may affect or appear to affect the design, conduct, reporting, review, or oversight of the human subjects research." ICOIs are of significant concern when an Institutional Financial Interest creates the potential for inappropriate influence over the research, particularly to the integrity of the research and the safety and care of patients enrolled in the research.

NYU Langone Health's policy is that it will not participate in a human subjects research project that involves a significant ICOI due to Institutional Financial Interests. Examples of situations that may give rise to a significant ICOI include:

- A clinical trial or other human subjects research that is greater than minimal risk, that involves testing, validating, or developing a product covered by an NYU or NYU Langone Health Intellectual Property Right; or
- A clinical trial sponsored by a for-profit company in which NYU or NYU Langone Health holds or proposes to hold an equity interest.

If the CIMU determines that a significant ICOI may exist, the CIMU, in consultation with the Office of General Counsel and NYU Langone Health's Executive Vice President and Vice Dean for Science, Chief Scientific Officer, will determine whether Compelling Circumstances exist to merit an exception and whether diligent efforts to eliminate the ICOI have not succeeded. If the CIMU determines Compelling Circumstances exist for NYU Langone Health's participation despite the Institutional Financial Interest, a conflict management plan will be issued and must be approved by the study's Principal Investigator before being adopted. The conflict management plan can include restrictions similar to those contemplated for individual conflict management plans, and additional restrictions on NYU Langone Health's institutional participation in the research.

For any human subjects research study where an ICOI exists, the IRB will not issue its final initial approval of the study before the CIMU has completed its review and evaluation of the ICOI as required under the *Institutional Conflicts Policy*. The IRB may not approve research protocols referred to the CIMU that have not

been approved by the CIMU or approve monitoring procedures or other conditions that are less restrictive than those imposed by the CIMU.

Upon completion of its review and evaluation, the CIMU will notify the IRB of its final determination of the ICOI review and, if applicable, will submit to the IRB the approved conflict management plan. Upon receipt of the agreed-upon conflict management plan, the IRB Chair (or designee) will review the conflict management plan prior to issuing the IRB's final initial approval of the project. The IRB may modify the plan to impose more stringent restrictions than those imposed by the CIMU in order to protect research subjects. IRB Operations must document completion of the review required under the *Institutional Conflicts of Interest Policy* in the applicable IRB protocol/study file, which will include retaining a copy of the final, approved conflict management plan.

16.10 SUBJECT RECRUITMENT

Investigators are responsible for recruiting research subjects in a manner that is fair, ethical and equitable. IRB approval is required for all study recruitment procedures and materials. Recruitment materials must be consistent with the IRB-approved protocol, accurate, and not coercive. If recruitment procedures contemplate concurrent enrollment of subjects in multiple ongoing studies, such procedures must be explicitly described in the relevant protocol(s). For specific information regarding recruitment materials, review and creation guidance, please see the *Informational Sheet regarding Advertisements and Recruitment Materials*. For specific information regarding recruitment materials, review and creation guidance, please see the *Informational Sheet regarding Advertisements and Recruitment Materials*.

RECRUITMENT INCENTIVES

Payment arrangements among sponsors, organizations, investigators, and those referring research subjects may place subjects at risk of coercion or undue influence or cause inequitable selection. Payment in exchange for referrals of prospective subjects from researchers/physicians (referred to as "finder's fees") is not permitted. Similarly, payments designed to accelerate recruitment that are tied to the rate or timing of enrollment (referred to as "bonus payments") are also not permitted.

PAYMENT TO SUBJECTS

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

JUSTIFICATION FOR PAYMENT

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

- substantiate that proposed payments are reasonable and commensurate with the expected contributions of the subject;
- state the terms of the subject participation and the amount of payment which should be incorporated in the informed consent form; and

- substantiate that subject payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure on the patient to volunteer for the research study.

IRB REVIEW

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

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

The NYU Langone Health IRBs prohibit:

- the entire payment to be contingent upon completion of the entire study; and
- compensation for participation in a trial in the form of a coupon offered by the sponsor that is good for a discount on the purchase price of the product being investigated once it has been approved for marketing.

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

PROCEDURES FOR DISBURSEMENT

Unless the study is confidential/of a sensitive nature, the NYU Langone Health Office of Business and Financial Services requires personal identifying information in order to issue checks payable through NYU Langone Health's Accounts Payable procedures, bank cards, or gift cards to subjects. The study's consent form must inform subjects that they will be asked to provide their social security number and verification of U.S citizenship or permanent resident status to receive payment. For confidential studies/studies of a sensitive nature, only the subject's name and address are required, but the Principal Investigator must keep an identity key in a secure place.

NYU Langone Health investigators should refer to NYU Langone Health's *Policy on Human Subjects Payments located* on the Research Policy Hub for additional and current guidance on acceptable payment methods and procedures.

16.11 INVESTIGATOR CONCERNS

Investigators who have concerns or suggestions regarding NYU Langone Health's human research protection should convey them to the Senior Director, HRP, Institutional Official or other responsible parties (e.g., Department Chair, NYU Langone Health's Chief Scientific Officer, Office of Research Compliance, Office of General Counsel) regarding the issue, when appropriate. The Senior Director will research the issue, and when deemed necessary, convene the parties involved to form a response for the investigator or make necessary procedural or policy modifications, as warranted. In addition, an NYU Langone IRB Chair will be available to address investigators' questions, concerns and suggestions for studies reviewed by the NYU Langone IRBs.

16.12 UPDATING CVS FOR NYU LANGONE HEALTH EMPLOYEES

CVs for the Principal Investigator and each member of the research team for a study are required for each new study submission, and are included in the relevant Research Navigator study record. An up to date CV is required for IRB review and must be uploaded for any NYU Langone Health employee in his/her Research Navigator person profile.

Effective February, 2019, any NYU Langone Health personnel who does not have a CV uploaded in a Research Navigator person profile associated with that individual will not be approved to be added to a study until the individual's person profile is updated. CVs should be updated every three (3) years in the Research Navigator person profile or whenever updates are made to the CV, whichever is sooner. Investigators may assign a designee to upload and manage his/her CV in person profile.

17. HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA)

The *Health Insurance Portability and Accountability Act of 1996* ("HIPAA") is an expansive federal law, only part of which is intended to protect the privacy of health care information. HIPAA required Congress to enact a health information privacy law by August 1999 and stated that if it did not act by then, which it did not, the U.S. DHHS must develop privacy regulations. HIPAA required the creation of a Privacy Rule for identifiable health information. The resulting Privacy Rule, finalized in August 2002, set a compliance date of April 14, 2003. While the main impact of the Privacy Rule will be on the routine provision of and billing for health care, the Privacy Rule also affects the conduct and oversight of research.

Investigators, researcher team members, IRB Operations staff, and IRB members as well as research administrators must be aware of HIPAA and the Privacy Rule.

The objective of the Privacy Rule is to protect the privacy of an individual's health care information. It creates a federal "floor" of protection so that every person in the U.S. has at least the same basic rights and protections, though some may have additional rights depending on state law. Protected Health Information ("PHI") collected and maintained by NYU Langone Health may not be used internally or disclosed to any outside person or organization for research purposes without prior approval of the IRB. NYU Langone Health researchers must also abide by all institutional/corporate policies regarding HIPAA privacy and security.

The following describes the procedures for conducting research at NYU Langone Health in accordance with HIPAA and the Privacy Rule.

17.1 DEFINITIONS

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

Authorization means, for purposes of this Policy, a detailed document that gives Covered Entities permission to (a) use PHI for specified purposes, which are generally for purposes other than treatment, payment, or health care operations, or (b) to disclose PHI to a third party specified by the individual whose PHI is to be disclosed.

COVERED ENTITY is the term applied to institutions that must comply with the Privacy Rule. These include:

- health plans (such as health insurance companies, health management organizations (HMOs), and government programs that pay for health care, e.g., Medicare and Medicaid);

- health care clearinghouses (including entities that process non-standard health information they may receive from another entity into a standard format, i.e., standard electronic format or data content, or vice-versa); and
- health care providers that transmit information in an electronic form in connection with a financial and administrative transaction for which the Secretary of the U.S. Department of Health and Human Services (HHS) has adopted a standard, such as electronic billing and fund transfers. Such providers include doctors, clinics, psychologists, dentists, pharmacies, and others.

COMMON RULE is the federal policy on human subject protection that provides for the primary source of regulation of human subject research.

DE-IDENTIFIED INFORMATION means health information that does not identify an individual and with respect to which there is no reasonable basis to believe that the information can be used to identify an individual. If information is de-identified, it no longer is subject to the Privacy Rule and exempt from HIPAA.

DELETION means the removal, erasing, or expunging information or data from a record.

DISCLOSURE means the release, transfer, provision of access to, or divulging in any other manner, information outside of the Covered Entity.

HEALTH INFORMATION means any information created or received by a health care provider or health plan that relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or payment for the provision of health care to an individual.

IDENTIFIABLE HEALTH INFORMATION is a subset of Health Information including demographic information collected from an individual and that (a) identifies the individual or (b) with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

LIMITED DATA SET is PHI that excludes specific direct identifiers of the individual or of relatives, employees or household members of an individual. A Limited Data Set can only be used for the purposes of research, public health, or healthcare operations, and disclosed for the purpose of research.

MINIMUM NECESSARY refers to the principle that any access should be limited to the minimum amount of information needed to accomplish the intended purpose of the use or disclosure.

PRIVACY BOARD is the term used to describe a board comprised of members of varying backgrounds and appropriate professional competencies, as necessary, to review individuals' privacy rights. It is only an alternative to an IRB for privacy issues. A Privacy Board cannot replace the IRB for Common Rule purposes.

PRIVACY ACT is a law that provides for the confidentiality of individually identified and retrieved information about living individuals that is maintained in a system of records and permits the disclosure of records only when specifically authorized by the statute. The Act provides that the collection of information about individuals is limited to that which is legally authorized, relevant, and necessary.

PRIVACY RULE enacted under HIPAA provides guidance on the use of PHI in the conduct of research. It imposes requirements on those involved in research, both individuals and institutions. "Privacy" refers to a person's desire to control the access of others to themselves. The evaluation of privacy involves consideration of how the Principal Investigator will access information from or about research subjects. The IRB members should know strategies to protect privacy interests relating to contact with potential subjects, and access to private information.

PROTECTED HEALTH INFOMRATION ("PHI") is individually identifiable health information transmitted or maintained electronically or in any other form or medium, except for education records or employment records, as excluded in the HIPAA Privacy Rule.

WAIVER OF AUTHORIZATION is a means of requesting approval from an IRB or Privacy Board rather than asking each research subject for an authorization to access subjects' PHI.

17.2 IMPACT OF HIPAA ON RESEARCH

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

NYU Langone Health is a Covered Entity under HIPAA. NYU Langone Health researchers who are working with PHI will be required to comply with the rules on HIPAA. The NYU Langone Health IRBs each act as the institution's Privacy Board.

The Privacy Rule permits Covered Entities to use or disclose PHI for research purposes when the individual who is the subject of the information authorizes the use or disclosure. For clinical research, Authorization must be sought in addition to informed consent. Authorization must also be sought for other research uses or disclosures of PHI that do not qualify for an IRB Waiver of Authorization (discussed below).

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

- An Authorization for use or disclosure of PHI for a research purpose may state that the Authorization does not expire, that there is no expiration date or event, or that the Authorization continues until the end of the research study;
- An Authorization for the use or disclosure of PHI for research may be combined with a consent to participate in the research, or with any other legal permission related to the research study, with the exception of research involving the use or disclosure of psychotherapy notes, which must be authorized separately; and
- Research Authorization forms must be filled out completely and accurately by the Principal Investigator, to ensure that all parties who require access to PHI for the research (including sponsors, contract research organizations, DSMBs, IRBs, etc.) are identified in the Authorization form and may receive the PHI. The combined Authorization/consent form should be completed by the Principal Investigator and submitted to the applicable NYU Langone Health IRB, for review and approval.

17.3 APPLICABILITY OF HIPAA ON RESEARCH

HIPAA defines "research" as "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge." This definition is identical with the one used in the Common Rule, which is separate federal legislation designed to protect human subjects involved in research. HIPAA describes privacy standards for protecting PHI; therefore it only applies to research that involves humans' (not animals') health information.

WAIVER OF AUTHORIZATION FOR USE OR DISCLOSURE OR PROTECTED HEALTH INFORMATION IN RESEARCH

Under the Privacy Rule, Covered Entities are permitted to use and disclose PHI for research with an individual's Authorization, or without individual's Authorization under limited circumstances. A Covered Entity may use or disclose PHI for research when presented with documentation that an IRB has granted a Waiver of Authorization request [see 45 CFR 164.512(i)(1)(i)]. This provision of the Privacy Rule might be used, for example, to conduct records research, epidemiological studies, or other research where de-identified data is unavailable or not suited to the research purpose.

REQUIRED WAIVER DOCUMENTATION

The waiver documentation presented to the Covered Entity must include the following:

- Identification of the IRB or Privacy Board and the date on which the alteration or Waiver of Authorization was approved;
- A statement that the IRB or Privacy Board has determined that the alteration or Waiver of Authorization, in whole or in part, satisfies the three criteria in the Privacy Rule;
- A brief description of the PHI for which use or access has been determined to be necessary by the IRB or Privacy Board;
- A statement that the alteration or Waiver of Authorization request has been reviewed and approved under either normal or expedited review procedures; and
- The signature of the IRB Chair or other member, as designated by the IRB Chair, or the Chair of the Privacy Board, as applicable.

CRITERIA FOR IRB APPROVAL OF WAIVER OF AUTHORIZATION

All of the following three criteria must be satisfied for the IRB to approve a Waiver of Authorization under the Privacy Rule.

(1) The use or disclosure of PHI involves no more than a minimal risk to the privacy of individuals, based on, at least, the presence of the following elements:
- an adequate plan to protect the identifiers from improper use and disclosure;
- an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
- adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of PHI would be permitted by this subpart.

(2) The research could not practicably be conducted without the Waiver of Authorization or alteration; and

(3) The research could not practicably be conducted without access to and use of the PHI.

PHI REVIEW TO PREPARATORY RESEARCH

The Privacy Rule permits a Covered Entity to use or disclose PHI to a researcher without Authorization or Waiver of Authorization for the limited purpose of a "review preparatory to research." Such reviews may be used to prepare a research protocol, or to determine whether a research site has a sufficient population of potential research subjects. Prior to permitting the researcher to access the PHI, the Covered Entity must obtain representations from the researcher that (a) the use or disclosure of the PHI is solely to prepare a research protocol or for similar purposes preparatory to research, (b) the researcher will not remove any PHI from the Covered Entity, and (c) PHI for which access is sought is necessary for the research purpose. Researchers should consult the Covered Entity regarding any forms or applications necessary to conduct a review preparatory to research.

Researchers conducting a review preparatory to research may not record information in identifiable form, nor may they use PHI that they receive to contact potential subjects, unless the investigator is also the

subject's treating physician. Because the Privacy Rule permits a Covered Entity to disclose PHI to the individual who is the subject of the information, covered health care providers and patients may continue to discuss the option of enrolling in a clinical research study without patient authorization.

Even when permitted by the Privacy Rule, however, any use of patient information for recruitment must comply with IRB policies relating to subject recruitment, as noted below.

- All human subjects research requires IRB review to determine either (a) Exempt status or (b) need for further review.

- Reviews preparatory to research that are permitted under HIPAA may or may not be human subjects research depending on the investigation being conducted.
  IRB review is not required only in the case where the proposed activity is review of a database by an individual who is entitled to access it, which database is intended to enumerate an available data set without reviewing PHI and where no PHI is recorded.

  For example: medical records may be queried for information such as: In the year XXXX how many patients had a discharge diagnosis of [indicate disease/diagnosis].
  IRB Privacy Board review is required for all other uses of PHI as indicated. If the research involves a de-identified data set, defined as a data set where all of the identifiers (as listed below) are removed, then a de-identified data set certification form must be completed, submitted for administrative review, and certified prior to accessing the data set. This activity also requires an IRB-determined exemption from review:
  (1) Names (full name or last name and initial(s))
  (2) Postal address information (geographical subdivisions smaller than a state including street, address, city, county, precinct, zip code, equivalent geocodes)
  (3) All elements of dates directly related to an individual, other than years
  (4) Telephone numbers
  (5) Fax numbers
  (6) E-mail addresses
  (7) Social Security numbers
  (8) Medical Record numbers
  (9) Health plan beneficiary numbers
  (10) Account numbers
  (11) Certificate/License numbers
  (12) Vehicle identifiers (including serial numbers, license plate numbers)
  (13) Device identifiers, serial numbers
  (14) Web URLs
  (15) IP address numbers
  (16) Biometric identifiers (e.g., finger prints, retinal or voice prints)
  (17) Full face photo images and any comparable photo images
  (18) Any other unique identifying numbers, characteristics, or codes other than the unique code assigned by the investigator to code the data (e.g., prescription numbers)

  IRB and Privacy Board review and approval is required prior to initiating research. Investigators are not authorized to contact potential research subjects identified in reviews preparatory to research unless they are directly responsible for care of the potential subject and entitled to PHI as a result of that duty. Principal Investigators who have previously obtained full consent and Authorization to contact a research subject as a result of a previously IRB-approved research project may contact his or her former research subjects provided that the subject agreed to be contacted for information on future research conducted by the same Principal Investigator or co-investigator (s).

RESEARCH ON PROTECTED HEALTH INFORMATION OF DECEDENTS

The protections of the Common Rule apply only to living human beings. By contrast, the Privacy Rule also protects the identifiable health information of deceased persons ("Decedents"). The Privacy Rule contains an exception to the Authorization requirement for research that involves the PHI of Decedents.

A Covered Entity may use or disclose Decedents' PHI for research if the Covered Entity obtains representations from the researcher (a) that the use or disclosure being sought is solely for research on the PHI of Decedents, and (b) that the PHI being sought is necessary for the research.

If requested by the Covered Entity, documentation of the death of the individuals about whom PHI is being sought must be obtained and provided.

Notification to the IRB is required for research involving Decedents' PHI. The Principal Investigator should submit the completed applicable IRB form, Application for Research on Decedent's Information, for IRB review when they intend to conduct research involving Decedents' PHI. The completed form should be sent via email to IRB Operations by contacting IRB-info@nyulangone.org. The IRB will confirm the use and return to the Principal Investigator a fully signed form. The Principal Investigator should file the signed form in the study records and provide the form as documentation of use and disclosure.

LIMITED DATA SETS WITH A DATA USE AGREEMENT

When a researcher does not need direct identifiers of individuals for a study but does require certain identifiable data elements that are normally not permitted in de-identified data, the Privacy Rule permits a Covered Entity to disclose a "Limited Data Set" to the researcher without Authorization or Waiver of Authorization, provided that a data use agreement has been signed between the researcher and Covered Entity. The Limited Data Set as defined by HIPAA is still considered to be PHI and is therefore still subject to the requirements of the Privacy regulations as it can include identifiable patient information, but it must exclude specified direct identifiers of the individual whose information is to be used, or of the individual's relatives, employers, or household members.

Specifically, all of the following 16 identifiers must be removed in order for the health information to be a Limited Data Set:

1. Names
2. Street addresses (other than town, city, state and zip code)
3. Telephone numbers
4. Fax numbers
5. Email addresses
6. Social Security numbers
7. Medical Record numbers
8. Health plan beneficiary numbers
9. Account numbers
10. Certificate/license numbers
11. Vehicle identifiers (including serial numbers, license plate numbers)
12. Device identifiers, serial numbers
13. Web URLs
14. IP address numbers
15. Biometric identifiers (e.g., finger prints, retinal or voice prints)
16. Full face photo images and any comparable images

Health information that may remain in a Limited Data Set includes:

- Dates such as admission, discharge, service, date of birth, date of death;
- City, state, five digit or more zip code; and
- Ages in years, months or days or hours.

The Privacy Rule requires that the data use agreement used in conjunction with the Limited Data Set contain provisions that:

- establish the permitted uses and disclosures of the Limited Data Set by the recipient, consistent with the purposes of the research, and which may not include any use or disclosure that would violate the Privacy Rule if done by the Covered Entity;
- limit who can use or receive the data;
- require the recipient to agree to the following:
    - not to use or disclose the information other than as permitted by the data use agreement or as otherwise required by law;
    - use appropriate safeguards to prevent the use or disclosure of the information other than as provided for in the data use agreement;
    - report to the Covered Entity any use or disclosure of the information not provided for by the data use agreement of which the recipient becomes aware. The recipient must agree to ensure that any of its agents, including a subcontractor to whom the recipient provides the Limited Data Set, agrees to the same restrictions and conditions that apply to the recipient with respect to the Limited Data Set; and
    - not to identify the information or contact the individual.
- requires that researchers who will be receiving Limited Data Sets under the data use agreement submit a signed copy of the Covered Entity's data use agreement to the applicable NYU Langone Health IRB for approval, prior to initiating the research.

TRANSITION PROVISIONS

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

- An Authorization or other express legal permission from an individual to use or disclose his/her PHI for the research;
- The informed consent of the individual to participate in the research; or
- A waiver of informed consent granted by the IRB for the research.

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

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

17.4 HIPAA AND DOCUMENT REQUIREMENTS

HIPAA documents include an Authorization form, a Waiver of Authorization form, Limited Data Set form, and a de-identification form. One of these documents must be used whenever PHI is utilized in the research.

17.5 PATIENT RIGHTS AND RESEARCH

Under HIPAA, patients have certain rights. Those that may affect research include the right to receive a Notice of Privacy Practices, the right to access, inspect, and receive a copy of one's own PHI, the right to request an amendment to one's own PHI, and the right to an accounting of certain disclosures of PHI that occur outside the scope of treatment, payment and health care operations that have not been authorized.

17.6 HIPAA AND EXISTING STUDIES

Any research subject enrolled in a study that uses PHI from a Covered Entity must sign a HIPAA- compliant Authorization form. This form is in addition to the existing Informed Consent document, and is federally required.

18. SPECIAL TOPICS

18.1 CERTIFICATE OF CONFIDENTIALITY

STATUATORY BASIS FOR PROTECTION

The Public Health Service Act §301(d), 42 U.S.C.§241(d) provides for protection against compelled disclosure of identifying information about subjects of biomedical, behavioral, clinical, and other research:

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

Certificates of Confidentiality ("CoCs") constitute an important tool to protect the privacy of research study subjects. CoCs are issued by the National Institutes of Health (NIH) to protect identifiable research information from forced disclosure. They allow the Principal Investigator and others who have access to research records to refuse to disclose identifying information of research subjects in connection with any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level.

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

CoCs are granted sparingly. The study's funding source, if any, is not relevant to the decision.

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

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

- information about sexual attitudes, orientation, practices;
- information about personal use of alcohol, drugs, or other addictive products;
- information about illegal conduct;
- information that could damage an individual's financial standing, employability, or reputation within the community;

- information in a subject's medical record that could lead to social stigmatization or discrimination; or
- information about a subject's psychological well-being or mental health.

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

The IRB may require Principal Investigators to apply for a CoC.

LIMITATIONS

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

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

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

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

APPLICATION PROCEDURES

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

Note: Effective October 1, 2017, CoCs will be automatically issued as a term and condition of the award for any NIH-funded project that uses identifiable, sensitive subject information that was ongoing on or after December 13, 2016.

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

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

For more information, see the NIH Certificates of Confidentiality Kiosk (https://humansubjects.nih.gov/coc/index.)

18.2 MANDATED REPORTING

This Policy addresses mandated reporter obligations in relation to human subjects research.

While any person may make a report if they have reasonable cause to believe that a child or elderly person has been or is being abused or neglected, New York State law mandates that certain persons must report

suspected child abuse or maltreatment, when, in their professional capacity, they are presented with reasonable cause to suspect child abuse or maltreatment. "Reasonable cause" to suspect child abuse or neglect means that based on one's observations of the evidence, professional training and experience, one believes that the parent or legal guardian has harmed or placed a child in danger of being harmed. When elder abuse in residential facilities is suspected, certain persons are required under New York State Law to report such cases to authorities as well.

NYU Langone Health policy requires that informed consent be obtained from all adult research subjects and assent from children involved as research subjects, in addition to the consent of their respective parents/legal guardians. In situations where conditions of abuse or neglect might be revealed, mandated reporters under New York State law should make themselves and their obligations known to parents of children under age 18, to subjects who are children, and to subjects who are potential victims of elder abuse or neglect.

New York Social Services Law § 413 states, in part:

> Sec. 1. (a) The following persons and officials are required to report or cause a report to be made in accordance with this title when they have reasonable cause to suspect that a child coming before them in their professional or official capacity is an abused or maltreated child, or when they have reasonable cause to suspect that a child is an abused or maltreated child where the parent, guardian, custodian or other person legally responsible for such child comes before them in their professional or official capacity and states from personal knowledge facts, conditions or circumstances which, if correct, would render the child an abused or maltreated child: any physician; registered physician assistant; surgeon; medical examiner; coroner; dentist; dental hygienist; osteopath; optometrist; chiropractor; podiatrist; resident; intern; psychologist; registered nurse; social worker; emergency medical technician; licensed creative arts therapist; licensed marriage and family therapist; licensed mental health counselor; licensed psychoanalyst; licensed behavior analyst; certified behavior analyst assistant; hospital personnel engaged in the admission, examination, care or treatment of persons; a Christian Science practitioner; school official, which includes but is not limited to school teacher, school guidance counselor, school psychologist, school social worker, school nurse, school administrator or other school personnel required to hold a teaching or administrative license or certificate; social services worker; director of a children's overnight camp, summer day camp or traveling summer day camp, as such camps are defined in section thirteen hundred ninety-two of the public health law; day care center worker; school-age child care worker; provider of family or group family day care; or any other child care or foster care worker; mental health professional; substance abuse counselor; alcoholism counselor; all persons credentialed by the office of alcoholism and substance abuse services; peace officer; police officer; district attorney or assistant district attorney; investigator employed in the office of a district attorney; or other law enforcement official.

Additional guidance should be obtained from the child protection coordinators at the social work department of each NYU Langone Hospitals site. Reports must be made as soon as abuse or maltreatment is suspected, and are be reported by telephone to the New York Statewide Central Register of Child Abuse and Maltreatment (SCR). For more information about how to report, see the Summary Guide for Mandated Reporters in New York State, available at http://ocfs.ny.gov/main/publications/Pub1159.pdf.

New York State Public Health Law §2803-d requires certain persons (i.e., physicians and their assistants or associates, nurses, social \workers, physical and occupational therapists, psychologists) to report suspected instances of abuse, neglect or mistreatment of a person residing in a nursing home when there is reasonable cause to believe that a person in the facility, other than another patient, is the cause of such physical abuse, neglect or mistreatment. Any other person may, but is not obligated by law, to report. Reports must be made

immediately by telephone and within 48 hours of discovery in writing. Reports must be made to the Department of Health, Office of Health Systems Management.

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

18.3 RESEARCH INVOLVING EMPLOYEES AND STUDENTS AS RESEARCH SUBJECTS

DEFINITIONS

EMPLOYEES, for purposes of this Policy, includes full-time, part-time, and temporary faculty, staff, and residents of NYU Langone Health.

STUDENT, for purposes of this Policy, includes graduate students, medical students, medical residents, fellows, post-doctoral fellows, and doctoral students enrolled in a program within NYU Grossman School of Medicine ("NYUGSoM") or NYU Grossman Long Island School of Medicine ("NYUGLISoM").

DIRECT RECRUITMENT refers to subject recruitment that involves study investigator(s) providing study-related announcements and/materials directly to specific communities (i.e., Employees or Students) or subjects.

INDIRECT RECRUITMENT refers to subject recruitment that is not directed by study investigator(s) to specific communities (i.e., Employees or Students) or subjects.

POLICY

Employees and Students of NYU Langone Health may be enrolled as research subjects in research conducted at NYU Langone Health. In situations where the research is designed to focus on or study Employees and/or Students and/or where the research contemplates recruitment using Direct Recruitment methods to recruit and enroll Employees and/or Students, additional measures are required to ensure that their participation in the research is entirely voluntary and that their decision-making is freely-informed. Additional safeguards may be required by the IRB to protect the rights and welfare of these subjects. The voluntary nature of Students' and/or Employees' participation is paramount and the researcher should ensure risk of coercion is mitigated. Students and Employees recruited as research subjects are more vulnerable to undue influence, as they may perceive their grades, employment, or other benefits to be dependent on their decision to participate in research. There may also be greater challenges related to maintaining confidentiality and privacy.

In addition to protection of Students and Employees as subjects, there may be other concerns about the research. If Employees or Students will be the focus of subject recruitment efforts or will involve Direct Recruitment methods, notification, review, and clearance by NYU Langone Health's Department of Human Resources (HR), the department of Graduate Medical Education, or Vilcek Institute of Graduate Biomedical Sciences, as applicable, will be required in addition to IRB approval of any such project. Studies that will have nurses as subjects are required to go to the NYU Langone Health Departments of Nursing, Center for Innovations in the Advancement of Care (CIAC) for a review of the protocol.

Employees and Students who participate in research as subjects do so in a capacity separate and apart from their status as an Employee or Student. Their status as an Employee or Student shall have no bearing on any decisions related to their participation in the research. by the investigator, or Students enrolled in the

investigator's own course or laboratory, such that the potential influence of the investigator in recruiting his/her own Employees or Students is minimized.

REQUIREMENTS FOR INCLUSION OF EMPLOYEES AND STUDENTS IN RESEARCH

SUBMISSIONS TO IRB

The Principal Investigator must indicate in the IRB/Research Navigator submission whether the research is expected to involve Direct Recruitment of Employees and/or Students. If so, the Principal Investigator must specify the following in the protocol:

- A sound justification/rationale for the inclusion of Employees and/or Students. For any research that contemplates Employees' and/or Students' recruitment and/or participation, the protocol must specifically include Employees and/or Students in the inclusion criteria and provide specific justification for including Employees and/or Students as potential subjects. The IRB will review the overall inclusion/exclusion criteria for the study to ensure the equitable selection of subjects, while considering specific concerns posed by enrolling Employees and/or Students as subjects. The IRB will assess the level of risk and likelihood of direct benefit to research subjects to determine whether the research is of significant importance and cannot reasonably be conducted without the enrollment of the Employees and/or Students.
- An outline of recruitment methods, including the informed consent process, and any other procedures that will be followed to minimize the appearance of coercion or undue influence of the Employees and/or Students. Research subjects must generally be recruited from a "broad base" of individuals meeting the conditions for the study unless IRB finds there is justification for narrowing the subject population to a specific community (i.e., Employees or Students), group or subset. See *Additional Considerations* for specific methods of recruitment that may be used.
- An outline of procedures that will be followed to mitigate the potential risk of compromised confidentiality and privacy of subjects who are Employees and/or Students. Enrollment of Employees and/or Students will proceed only where the IRB determines that the study design includes adequate procedures and safeguards to minimize inherent concerns of coercion and undue influence, and to adequately address any confidentiality concerns.

DUTIES OF THE IRB

In addition to all other responsibilities prescribed for the IRB in NYU Langone Health *IRB Review Process* sections of this Policy manual, the IRB will review research involving Employees and Students and approve such research only if it finds that:

- Recruitment efforts are not directed solely to Employees or Students (individuals or groups) on the basis of convenience when they would not otherwise be appropriate for inclusion (e.g. an investigator's study team). In rare cases, the IRB may grant an exception to a subset of Employees or Students if the research directly relates to Employees in a particular department, or if the research directly relates to Students in a particular course. For example, if the research is intended to examine teaching methods in a particular course taught by the investigator. When the IRB determines there is justification for narrowing recruitment to a specific community (i.e., Employees or Students), the study's recruitment plan must include additional strategies to ensure voluntary participation when subjects may include Employees directly supervised.

- The proposed recruitment methods do not involve procedures that could be coercive or unduly influence potential subjects.
- Other study procedures adequately address confidentiality concerns, and mitigate risks of compromised confidentiality and privacy. Where applicable, the Principal Investigator should consider the necessity for a Certificate of Confidentiality ("CoC") where the research will delve into topics of mental health, drug/alcohol abuse, sexual behavior, or sensitive areas. Principal Investigators are responsible for submitting CoCs to the IRB.
- The informed consent form must include language that subjects' employment, academic status or grades will not be affected by their decision whether or not to participate or withdraw their consent. Researchers must emphasize the same during the informed consent process.
- All other IRB and NYU Langone Health policies applicable to the protection of human subjects in research, including but not limited to HIPAA and protections for other vulnerable populations, will apply.

ADDITIONAL CONSIDERATIONS: RECRUITMENT METHODS

Recruitment methods that are "passive" in nature, thus requiring the Employee or Student to reach out regarding participation in the research, are preferred in order to address voluntariness concerns. Acceptable methods to address these concerns include, but are not limited to, the following:

> (1) recruitment by a someone unassociated with the research and not in a supervisory relationship with an Employee,
> (2) flyers whose content is IRB-approved and are posted in NYU Langone Health campus areas accessed only by Employees or Students in a manner and locations as permitted by Real Estate Development and Facilities (RED+F), and specific department policies and guidelines,
> (3) NYU Langone Health-wide e-mails to specific listserv groups in which Employees and Students are provided contact information to receive more information[1], and/or
> (4) other methods that require an Employee or Student to initiate contact with the study's investigator(s) and to self-identify as an interested subject in a way that maintains their confidentiality, rather than methods by which an investigator approaches or solicits specific Employees or Students.

Use of broadcast e-mails through the Office of Communications and Marketing is not an acceptable method of recruitment under this Policy. Principal Investigators seeking approval to e-mail study announcements or recruitment materials to Employees and Students through broadcast e-mail must provide justification in the protocol for why this method is necessary. Exceptions for Employees and/or Students may be granted in limited circumstances by HR, the department of Graduate Medical Education, or Vilcek Institute of Graduate Biomedical Sciences, as applicable. Regardless of IRB approval of such an exception, the Office of Communications and Marketing has the authority to decide whether or not to grant a request for broadcast e-mail.

OTHER CONSIDERATIONS SPECIFIC TO INCLUSION OF EMPLOYEES

Employees recruited for research may be considered vulnerable to undue influence and coercion. An Employee who feels unable to fully exercise free choice in their decision to participate, due to the belief that their decision may affect (favorably or unfavorably) their performance evaluations, advancement opportunities, or other employment-related decisions, may feel compelled to participate in a research study.

Research that includes Employees as subjects also introduces unique confidentiality considerations. Even if research data will not be shared with their employer, Employees may feel compromised by the possibility their employer will know about their participation in the study. Workplace conditions may make it difficult for investigators to keep the Employee's participation confidential. This poses risks to the Employee, particularly where there is stigma associated with the condition or question being studied.

Methods to address these concerns include, but are not limited to, the following:

- Potential subjects will be informed in both the informed consent form and during the informed consent process of the extent to which their medical information and/or research data may be accessible to supervisors or others not directly involved in the research.
- An Employee must never be required to enroll in or to continue participation in research as a condition of their employment. Enrollment in, or continuance of, research participation must never be a factor in any employment-related decision.
- Investigators may not review or use Employees' Occupational Health records for research without the prior approval of the IRB. For research where the IRB does approve use of Employees' Occupational Health records, investigators must not access or use for research unless the Employee has given their authorization to use their Occupational Health records. No exceptions will be made for this requirement.
- Research should be conducted outside of the Employee's work areas and regular work hours when possible to minimize potential risks in breach of confidentiality.

OTHER CONSIDERATIONS SPECIFIC TO INCLUSION OF STUDENTS

The Principal Investigator must consider strategies for ensuring that Student participation in research is voluntary and free of undue influence, especially when the subjects are Students who receive instruction directly from the Principal Investigator or co-investigator(s). Students may feel that their participation in research is necessary as part of their academic requirements, or that their failure to participate will negatively impact their relationship and academic and professional opportunities with the instructor/investigator or NYU Langone Health in general.

Research that includes Students as subjects also raises special concerns about protection of their confidentiality and privacy interests. Classroom and laboratory conditions may make it difficult for investigators to keep an individual's participation confidential, which could pose risks to the Student-subject, e.g., when stigma is associated with the condition or question under study or when peer pressure is a component of the research.

A Student must never be required to participate in research for course credit. Any aspect of the Student-instructor/investigator relationship including the Student's grades, potential letters of recommendation, and other decisions made by the instructor/investigator must not be impacted by the Student's decision whether or not to enroll or to continue their participation in research.

A record of the participation of an NYUGSoM or NYUGLISoM Student must not be linked to an academic record.

The following additional safeguards may address concerns specific to Students:

- The informed consent form must include language that neither the Student's academic status nor grades will be affected by their decision to participate in research. Researchers shall emphasize the same during the informed consent process.
- Potential subjects will be informed in both the informed consent form and during the informed consent process of the extent to which their medical information and/or research data may be accessible to instructors or others not directly involved in the research.

- Research should be conducted outside of classroom or laboratory hours to minimize potential risks in breach of confidentiality.
- When entering a classroom or laboratory to conduct research, for instance, to administer a survey, investigators must do so at the end of the class period to allow non-participating Students the option of leaving the classroom or laboratory, thereby alleviating pressure to participate.

Additional privacy protections for Students are provided by federal regulations. If a study proposes to use Student education records for research, it must comply with the requirements of the Family Educational and Rights Privacy Act (FERPA). Investigators may only access Student records for research (for example, grades, assignments, term papers, etc.) with the prior written permission of the Students if they are over the age of 18. "Education record" is defined by FERPA as any record that is directly related to a Student and contains personally identifiable information and is maintained by the university or party acting on behalf of the university. While there may be case by case exceptions to FERPA, the FERPA policy of each institution in which a study will be conducted should be considered and investigators must follow that institution's FERPA policy, in addition to the IRB's requirements.

OTHER REQUIREMENTS: ANCILLARY REVIEW

For any study identified as one in which Employees or Students will be the focus of subject recruitment efforts or one that requires Direct Recruitment of Employees or Students, and may otherwise be of concern to the institution, NYU Langone Health's Department of Human Resources (HR), the department for Graduate Medical Education (GME), and the Associate Dean for Biomedical Sciences (for Ph.D. students) as applicable, and the study's Principal Investigator and research team will receive a notification through the Research Navigator system. Ancillary review by the applicable department (HR, GME, Vilcek Institute of Graduate Biomedical Sciences (Vilcek)) is required in addition to IRB approval of any such project.

An ancillary review status will be generated in the study record. The applicable ancillary review department will have access, for its review, the study details including the study protocol, consent form, advertisements, and any other relevant study documents. This ancillary department review may be conducted in parallel with the IRB's review of the study. This ancillary review is not required for studies which involve only Indirect Recruitment of individuals who are NYU Langone Health Employees or Students.

The Principal Investigator is responsible for ensuring that the appropriate NYU Langone Health department (HR, GME,Vilcek) has reviewed and approved the study before Direct Recruitment of any NYU Langone Health Employees or Students in research. The clearance by the ancillary department will be documented in the Research Navigator/MyStudies record.

Prior written consent of the HR department is also required for direct use of NYU Langone Health Employee data for research purposes, in addition to written consent of the Employees whose data is to be used.

Once a study is approved by the IRB and the appropriate department has completed its ancillary review, if recruitment methods will involve use of NYU Langone email (research distribution lists), or flyers and other postings, the Principal Investigator will submit additional information to other departments and committees as applicable, such as the Office of Science and Research for use of research distribution email lists, and/or RED+F for use of flyers and other postings.

The Office of Research Communication in the Office of Science and Research will require an IRB approval letter for the study and verification of review and clearance by HR, the GME, and/or the Associate Dean of Biomedical Sciences (as applicable) before permitting the study team to send email to those on the list provided by the respective office.

Further related guidance for Principal Investigators can be found in the IRB Guidance *Inclusion of Students and Employees in Research.*

[1] **E-mails to listserv groups:** E-mails must be approved by NYU Langone Health's Office of Communications and Marketing. Principal Investigators may utilize e-mail listservs, which include individuals within a specific distribution group. The Principal Investigator should contact NYU Langone Health's Office of Science and Research for assistance in identifying appropriate listserv groups and sending recruitment materials or study announcements.

18.4 ORAL HISTORY ACTIVITIES

The following Policy is based on guidance received from the OHRP:

> A decision whether oral history or other activities solely consisting of open ended qualitative type interviews are subject to the policies and regulations outlined in an institution's FWA and HHS regulations for the protection of human research subjects (45 CFR 46) is based on the prospective intent of the investigator and the definition of "research" under HHS regulations at 45 CFR 46.102(d): "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

Specifically, for the purposes of this Policy, the evaluation of such activities hinges upon whether:

- The activity involves a prospective research plan which incorporates data collection, including qualitative data, and data analysis to answer a research question; and
- The activity is designed to draw general conclusions (i.e., knowledge gained from a study may be applied to populations outside of the specific study population), inform policy, or generalize findings.

In order to be subject to NYU Langone Health's human research protections policies, the proposed activity must meet both of the above standards.

General Principals for evaluating Oral History type activities:

- Oral history activities, such as open ended interviews, that only document a specific historical event or the experiences of individuals without intent to draw conclusions or generalize findings would not constitute "research" as defined by HHS regulations 45 CFR part 46.

> Example: An oral history video recording of interviews with holocaust survivors is created for viewing in the Holocaust Museum. The creation of the videotape does NOT intend to draw conclusions, inform policy, or generalize findings. The sole purpose is to create a historical record of specific personal events and experiences related to the Holocaust and provide a venue for Holocaust survivors to tell their stories.

- Systematic investigations involving open-ended interviews that are designed to develop or contribute to generalizable knowledge (e.g., designed to draw conclusions, inform policy, or generalize findings) would constitute "research" as defined by HHS regulations at 45 CFR part 46.

> Example: An open ended interview of surviving Gulf War veterans to document their experiences and to draw conclusions about their experiences, inform policy, or generalize findings.

- Oral historians and qualitative investigators may want to create archives for the purpose of providing a resource for others to do research. Since the intent of the archive is to create a repository of information for other investigators to conduct research as defined by 45 CFR part 46, the creation of such an archive would constitute research under 45 CFR part 46.

> Example: Open ended interviews are conducted with surviving Negro League Baseball players in order to create an archive for future research. The creation of such an archive would constitute research under 45 CFR part 46 since the intent is to collect data for future research.

Principal Investigators are advised to consult with the IRB Operations regarding whether their oral history project requires IRB review.

18.5 GENETIC STUDIES

Since human genes are the sequence instructions to make all human proteins, genetic studies can lead to a molecular description of normal physiological function. Likewise, defects (mutations) in individual genes can lead to pathology. This is a major current area of health research, although the potential power of genetic research is also the inherent risk. In particular, patients and family members can learn of ominous mutations prior to disease symptoms. Thus, genetic information, not specifically solicited by the subject, could be the first warning sign of a troubled future. Furthermore, such mutations can be carried through subsequent generations, affecting as yet unborn descendants; and potential illness can be predicted even for family members, un-enrolled and unaffiliated with the research protocol. Although of high predictive value when proven, un-validated results of genetic experiments can still cause actual psycho-social hardship even leading to financial loss.

PRIVACY AND CONFIDENTIALITY

In human subjects research using genetic testing, the actual physical interventions involved are usually minor, and would ordinarily be reviewed under the Minimal Risk categories of the federal regulations as just a blood draw. However, the IRB Board, when reviewing any studies with genetic testing, must also consider the various psychosocial and financial risks. This includes examining the procedures in place to preserve

confidentiality of study information, and subject identity. It also includes assessing the potential consequences of inadvertent disclosure.

The procedures that could be used to preserve confidentiality include: keeping the test results in the research records and out of the clinical patient charts, and doing the testing in research laboratories where results could not be relied on for clinical decision making or provided to insurance companies as validated health records.

Encoding data such that individual identity is separate from medical/genetic information (de-identification) is a key element in dealing with all research data that could suggest, among other things, that:

- a subject may eventually suffer a serious loss of abilities related to his/her career;
- the subject might incur higher than usual health care costs;
- the subject has a statistically lower life expectancy; or
- the subject's ability to procreate and perform socially may become impaired.

DIAGNOSTIC STATUS AND TYPES OF TESTS

In assessing these risks, aside from considering the predictive confidence of the information and its health implications, one should also consider the current diagnostic status of the subject. For example, genetic test studies that are confirmatory of an established diagnosis (testing the test), have much lower risk then when they are predictive in the absence of any symptoms. Also, gene expression studies that are mechanistic in nature may not directly relate to a genetic mutation that could be inherited.

Pharmacogenomic studies, for example, could help chose the most effective therapy, or inform the subject that the available therapies would or would not be effective–thus conferring a range of risks and benefits that must be considered.

FEDERAL VS STATE LAW

Thus, federal human subjects regulations treat genetic testing to the extent that risks associated with breach of confidentiality, financial harm and psychosocial consequence must all be analyzed along with the potential benefits of the study. However, New York State (NYS) law includes some specific provisions which must be applied whenever human subjects participate in a genetic testing trial located in NYS, where NYS law defines a "genetic test".

The definition of "genetic test" is less important in the context of federal laws on genetic testing because there is no "genetic testing article". Both sets of laws apply to all subjects in NYU Langone Health clinical research.

In Section 79-L.1.(a) of the NYS Civil Rights Law:

> "Genetic test" shall mean any laboratory test of human DNA, chromosomes, genes, or gene products to diagnose the presence of a genetic variation linked to a predisposition to a genetic disease or disability in the individual or the individual's offspring; such term shall also include DNA profile analysis. "Genetic test" shall not be deemed to include any test of blood or other medically prescribed test in routine use that has been or may be hereafter found to be associated with a genetic variation, unless conducted purposely to identify such genetic variation.

While "gene product" could be implied to refer to either proteins or RNA, expression studies often are not designed to "diagnose the presence of a genetic variation linked to a predisposition to a "genetic disease". In any case, there are specific requirements that need to be incorporated in the informed consent form if the study is determined to be a genetic test study, and these apply in addition to the elements of consent for general human subjects research defined under federal law in the Code of Federal Regulations (45 CFR 46.116). These additional requirements include (Section 79-L.2.(b). of the NYS Civil Rights Law):

1) a general description of the test
2) a statement of the purpose of the test; … {including}… a statement indicating that the individual may wish to obtain professional genetic counseling prior to signing the informed consent.
3)a statement that a positive test result is an indication that the individual may be predisposed to or have the specific disease or condition tested for and may wish to consider further independent testing, consult their physician or pursue genetic counseling;
4) a general description of each specific disease or condition tested for;
5) the level of certainty that a positive test result for that disease or condition serves as a predictor of such disease - If no level of certainty has been established, this subparagraph may be disregarded;
6) the name of the person or categories of persons or organizations to whom the test results may be disclosed;
7) a statement that no tests other than those authorized shall be performed on the biological sample and that the sample shall be destroyed at the end of the testing process or not more than sixty days after the sample was taken, unless a longer period of retention is expressly authorized in the consent; and
8) the signature of the individual subject of the test or, if that individual lacks the capacity to consent, the signature of the person authorized to consent for such individual.

Furthermore in Section 79-L.2.(f), NYS law indicates that to keep a genetic sample for more than sixty (60) days, the approval of an IRB is required. It acknowledges further that genetic research often cannot provide the information in (3), (4) and (5) above, and that this is acceptable.

The presence of these affirmative requirements for informing the subjects of the purpose and procedures of the genetic tests do not preclude more open ended use of de-identified genetic material at a later time, provided that certain provisions are followed and that the subject did not specifically disallow this:

> 9. Notwithstanding the provisions of subdivisions two and ten of this section, samples may be used for tests other than those for which specific consent has been obtained, for purposes of research conducted in accordance with applicable law and regulation and pursuant to a research protocol approved by an institutional review board, provided the individuals who provided the samples have given prior written informed consent for the use of their sample for general research purposes and did not specify time limits or other factors that would restrict use of the sample for the test, and
>
> (1) the samples have been permanently stripped of identifying information; or
>
> (2) a coding system has been established to protect the identity of the individuals who provided the samples, and an institutional review board has reviewed and approved the procedures for the coding system.

Thus, in terms of the written law, there are more stringent requirements for IRB Full Board review for genetic studies under NYS in contrast to federal law.

Furthermore, the DHHS, in an advisory publication, has listed a variety of specific issues which must be dealt with in the consent form (and the review process), including:

- what data (including its reliability and significance) will be provided to the subject and when;
- that subjects may obtain information about themselves or family members which may make them uncomfortable, and likewise family members may be privy to the same information;
- that actions taken may compromise their privacy, insurability and result in financial loss;
- a list of assurances about safeguards to prevent loss of privacy;
- the rights subjects retain over tissue samples and medical information, including the consequences of withdrawing from the study; and
- any potential costs associated with participation.

Other state laws may have different requirements which must be applied for genetic testing studies conducted in those jurisdictions.

RECRUITMENT FOR INDIVIDUAL OR PEDIGREE ANALYSIS STUDIES

A "pedigree analysis study" refers to the study of an inherited trait or disease in a group of related individuals to assess patterns and characteristics of the trait/disease, and to determine if there is a potential genetic basis for the trait/disease.

In genetic studies, confidentiality (the obligation of institutions to appropriately use restricted information once disclosed to them) and respect for privacy (the right to be left alone) begins with the recruitment process.

Contacting an individual to solicit participation in a genetic study can produce stress in the individual and should be done by the physician treating the patient for their related illness. However, this is often not possible for pedigree analysis studies, where it is desired to recruit family members. In such cases, the current subject under treatment or enrolled in the study (proband) should be used to contact the family members and assess their interest in being contacted.

There is additional legal basis for protecting the privacy of third parties in NYS law, which acts decisively in this regard. NYS Civil Rights Law, Section 79-L, 3(b) states:

> No person who lawfully possesses information derived from a genetic test on a biological sample from an individual shall incorporate such information into the records of a non-consenting individual who may be genetically related to the tested individual; nor shall any inferences be drawn, used, or communicated regarding the possible genetic status of the non-consenting individual.

Nonetheless instances may develop where unsolicited disclosure to a proband's family member of results from genetic testing is necessary, and the need to violate confidentiality must be considered. The conditions under which this is acceptable require all of the following:

- The subjects are at risk of serious harm;
- The harm can be ameliorated; and
- Only information necessary for amelioration is communicated.

SUMMARY

The following questions are useful in when reviewing genetic studies. In studies involving genetic testing, several questions need to be addressed, including:

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

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

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

RESEARCH INVOLVING CODED PRIVATE INFORMATION OR BIOLOGICAL SPECIMENS

This Policy is based on the Office of Human Research Protection ("OHRP") guidance document entitled *Coded Private Information or Specimens Use in Research, Guidance* (October 16, 2008 https://www.hhs.gov/ohrp/regulations-and-policy/guidance/research-involving-coded-private-information/index.html). This OHRP document:

- Provides guidance as to when research involving coded private information or specimens is or is not research involving human subjects, as defined under Health and Human Services ("HHS") regulations for the protection of human research subjects [45 CFR part 46].
- Reaffirms OHRP policy that, under certain limited conditions, research involving **only** coded private information or specimens is not human subjects research.
- Provides guidance on who should determine whether human subjects are involved in research.

For purposes of this Policy, *coded* means that:

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

Under the definition of "human subject" in this IRB Policies and Procedures document, obtaining identifiable private information or identifiable specimens for research purposes constitutes human subjects research.

For purposes of this Policy, "**obtaining**" means receiving or accessing identifiable private information or identifiable specimens for research purposes. This includes an investigator's use, study, or analysis for research purposes of identifiable private information or identifiable specimens already in the possession of the investigator.

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

Research involving only coded private information or specimens does not constitute involve human subjects research under this Policy if the following conditions are both met:

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

   and

2. The investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens pertain because, for example:
   - the key to decipher the code is destroyed before the research begins;
   - the investigators and the holder of the key enter into an agreement (data use agreement) prohibiting the release of the key to the investigators under any circumstances, until the individuals are deceased (Note: the HHS regulations do not require the IRB to review and approve this agreement);
   - there are IRB-approved written policies and operating procedures for a repository or data management center that prohibit the release of the key to the investigators under any circumstances, until the individuals are deceased; or
   - there are other legal requirements prohibiting the release of the key to the investigators, until the individuals are deceased.

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

- unexpectedly learn the identity of one or more living individuals, or
- for previously unforeseen reasons now believe that it is important to identify the individual(s).

If, as a result, the investigator knows, or may be able to readily ascertain, the identity of the individuals to whom the previously obtained private information or specimens pertain, then the research activity then would be deemed to be human subjects research. Unless this human subjects research is determined by the IRB to be exempt (See Exempt Research), IRB review of the research would be required. The investigator would also be required to obtain informed consent of the subjects also would be required unless the IRB approves a waiver of informed consent (See Waiver of Informed Consent).

The Principal Investigator in consultation with the IRB Chair or Senior Director, HRP will determine if the research involving coded information or specimens is human subjects research and requires IRB review. If the request for consultation is verbal (by phone or in person) or by email, it is the Principal Investigator's responsibility to maintain documentation of such a decision. If the Principal Investigator submits a formal request for determination in writing, the request must include sufficient documentation of the activity to support the determination. The formal submissions will be responded to in writing and a copy of the submitted materials and determination letter/email will be kept on file by IRB Operations.

18.6 CASE REPORTS REQUIRING IRB REVIEW

A "**SINGLE CASE REPORT**" refers to the external reporting (e.g., publication or poster/verbal presentation) of an interesting clinical situation or medical condition of a single patient. Case reports normally contain detailed information about an individual patient and may include demographic information and information on diagnosis, treatment, response to treatment, follow-up after treatment, as well as a discussion of existing relevant literature. The patient information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience.

A "***CASE SERIES***" refers to the external reporting (e.g., in a publication or poster/verbal presentation) of an interesting clinical situation or medical condition in a series of patients (i.e., more than one patient). A case series usually contains detailed information about each patient and may include demographic information and information on diagnosis, treatment, response to treatment, follow-up after treatment, as well as a discussion of existing relevant literature. The information used in the report must have been originally collected solely for non-research purposes as the result of a clinical experience.

In general, anecdotal reports on a single patient or series of patients seen in one's own practice and a comparison of these patients to existing reports in the literature is not research and does not require IRB approval. Going beyond one's own practice to seek out and report cases seen by other clinicians, however, creates the appearance of a systematic investigation with the intent to contribute to generalizable knowledge. Therefore, the latter activity should be considered research and requires IRB approval.

18.7 INTERNATIONAL RESEARCH

The IRB will review all NYU Langone Health research utilizing human subjects that is conducted internationally to assure adequate provisions are in place to protect the rights and welfare of the subjects.

Approval of research is permitted if "the procedures prescribed by the foreign institution afford protections that are at least equivalent to those provided in [45 CFR 46]."

All policies and procedures that are applied to research conducted domestically should be applied to research conducted in other countries, as appropriate.

The IRB must receive and review the foreign institution or site's IRB review and approval of each study prior to the commencement of the research at the foreign institution or site.

For federally funded research, approval of research for foreign institutions or sites "engaged" (as defined in Section 3, Definitions) in research is only permitted if the foreign institution or site holds an Assurance with OHRP and local IRB review and approval is obtained.

Approval of research for foreign institutions or sites "not engaged" in research is only permitted if one or more of the following circumstances exist:

- When the foreign institution or site has its own established IRB or independent ethics committee ("IEC"), the NYU Langone Health Principal Investigator must obtain approval to conduct the research at the "not engaged" site from the site's IRB/IEC or provide documentation that the site's IRB/IEC has determined that approval is not necessary for the Principal Investigator to conduct the proposed research at the foreign site.
- When the foreign institution or site does not have an established IRB/IEC, a letter of cooperation must be obtained demonstrating that the appropriate institutional or oversight officials are permitting the research to be conducted at the foreign site.

IRB approval for the NYU Langone Health Principal Investigator to conduct research at the foreign institution or site is contingent upon the IRB receiving documentation of the foreign site's IRB/IEC determination, or letter of cooperation, as applicable.

It is the responsibility of the NYU Langone Health Principal Investigator and the foreign institution or site to assure that the institution/site's resources and facilities are appropriate for the nature of the research activities.

It is the responsibility of the NYU Langone Health Principal Investigator and the foreign institution or site to confirm the qualifications of the researchers and research staff for conducting the research activities in that country(ies).

It is the responsibility of the NYU Langone Health Principal Investigator and the foreign institution or site to ensure that the following activities will occur:

- Initial review, continuing review, and review of modifications by the appropriate IRB/IEC or other institutional or oversight officials;
- Post-approval monitoring of the foreign institution or site; and
- Handling of complaints, non-compliance and Unanticipated Problems involving risk to subjects or others.

The IRB will not rely on a local ethics committee that does not have documented policies and procedures for the activities listed above.

It is the responsibility of the NYU Langone Health Principal Investigator and the foreign institution or site to notify the IRB promptly if a change in research activities alters the foreign site's engagement in the research (e.g., performance site "not engaged" begins consenting research subjects, etc.).

The IRB will consider local research context when reviewing international studies to assure that protections are in place that are appropriate to the setting in which the research will be conducted, including knowledge of local laws and cultural context.

In the case where there is no local IRB review, the IRB may require an expert consultant, either from the local country where the research is conducted or from an international organization, with the expertise or knowledge required to adequately evaluate the research in light of local context.

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

MONITORING OF APPROVED INTERNATIONAL RESEARCH

The IRB is responsible for the ongoing review of international research conducted under its jurisdiction through the continuing review process in accordance with all applicable federal regulations. When the IRB

and a local ethics committee will both be involved in the review of research, there is a plan for coordination and communication with the local ethics committees.

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

18.8 EMBRYONIC STEM CELL RESEARCH

Under NYU Langone Health's Policy on Human Stem Cell Research (NYU Langone Health Policy #ESCRO-1), NYU Langone Health regulates the use of human embryonic stem cells and other human stem cells in research, and the derivation for research, to assure compliance with all applicable laws, rules and regulations and to ensure that all such research is performed ethically. Certain activities relating to human stem cells, such as human reproductive cloning and research requiring the breeding of animals into which human embryonic stem cells have been introduced, are expressly prohibited.

All other research using human stem cells at NYU Langone Health is subject to the oversight and approval of NYU Langone Health's Embryonic Stem Cell Research Oversight ("ESCRO") Committee. The ESCRO Committee is also charged with maintaining a registry to document the source of any human embryonic stem cell lines being used in research at NYU Langone Health.

The composition, duties and responsibilities of the ESCRO Committee are distinct and separate from the IRB. Review and approval of the NYU Langone Health ESCRO Committee is therefore required in addition to the IRB's approval prior to commencement of applicable research at NYU Langone Health. The Policy on Human Stem Cell Research provides that, to the extent practicable, the subject matter of the ESCRO Committee's review should not overlap with the subject matter of the IRB's review.

18.9 COMMUNITY BASED RESEARCH

Where research is being conducted by or under the auspices of NYU Langone Health in communities, NYU Langone Health Principal Investigators are encouraged to involve members of the community in the research process, including the design and implementation of the research and the dissemination of results when appropriate. NYU Langone Health's Community Engagement and Population Health Research (CEPHR) program at the Clinical and Translational Sciences Institute ("CTSI") works with community members, health and social service providers, community-based organizations, research investigators, and policymakers to develop, adapt, and advance evidence-based health interventions in real-world healthcare and community settings. As part of the CTSI, CEPHR provides training and education necessary for research faculty members, post-doctoral researchers, health professionals, community providers, community members, and students to engage in translational research and to strengthen the relationships among these stakeholder groups.

CEPHR convenes the CTSI's Community Advisory Board (CAB). This group represents a diverse cross-section of New York City's ethnic communities, government, healthcare community, social services, and neighborhoods and boroughs. CAB's mission is to create healthier communities and multidirectional, equal, and reciprocal partnerships among the communities of New York City, NYU Langone Health, and NYC Health + Hospitals through participatory and sustainable methods of research, education, and advocacy.

The document "Guidance: Conducting Community-Engaged Research" provides further guidance on community based research.

When reviewing community-based research, the IRB will use the questions in the above-mentioned document as part of its evaluation of the research. The IRB will work in close collaboration with CEPHR to provide guidance on the issues related to the protection of human subjects in community based research.

18.10 INSTITUTIONAL POLICY ON RETURN OF INCIDENTAL FINDINGS FROM RESEARCH

DEFINITIONS

ANALYTICALLY VALID means a result from a test that is both confirmed and reproducible; for example, the result of a test performed in a laboratory or other facility with established procedures to ensure reproducibility.

Incidental Findings may be Analytically Validated through various methods including:

- A laboratory certified under the Clinical Laboratory Improvement Amendments (CLIA);
- A test conducted using FDA-approved devices or assays; and/or
- Consultation with a licensed expert (e.g., a radiologist, physician, a clinical geneticist).

CLINICALLY SIGNIFICANT means a finding or information would have the effect of changing a patient's diagnosis or treatment plan.

INCIDENTAL FINDING means a discovery concerning an individual research subject that:

(1) Is discovered in the course of research;
(2) Is **beyond or unrelated** to the results of the research required to achieve the primary aims of the study (e.g., a genetic research study that uncovers a finding beyond the ACMG 59 genes); and
(3) Has **potential** safety, health, reproductive, welfare, or psychiatric importance for the subject.

Examples:

- Possible brain tumor or vascular malformation found on a MRI scan.
- Lab test abnormality found as part of screening test for a clinical trial or for baseline physiologic data on a "healthy" control subject.
- Possible genetic abnormality or risk factor for future disease, response to medications, or carrier status.
- Discovery of non-paternity determined by genetic testing of parents.

MEDICALLY ACTIONABLE means findings or results would prompt clinical action by the subject's medical provider because there is an established medical/therapeutic intervention, preventative approach, or other actions (e.g., changes in medication) available that could have the potential to change the clinical course of the subject's disease or provide important pharmacogenetic information that is likely to impact future care.

POLICY BACKGROUND AND PURPOSE

Due to advances in imaging, genetic and genomic research technology, it is becoming increasingly common for findings to be discovered that are incidental to the research which could impact the health of a subject or of their family members. Principal Investigators must consider the possibility of such findings as part of their assessment of the risks and benefits of research participation, and have a plan for reporting of such findings.

Studies that generate secondary information about subjects' health may uncover information with immediate or possible future health implications, and could be helpful in directing the subject's clinical care. In some cases, research test results (such as those from a research genetic test) may not provide a direct correlation to a specific risk, or the test may not have undergone the scrutiny of a controlled research study to determine the value of the information that is generated. Being informed of a finding uncovered in research may thus raise concerns for subjects if the results were shared, including:

- Effect on access to or retention of benefits or entitlements (e.g., health, life or disability insurance, employment);
- Stigmatization: within or outside the subject's family, possibility of altered family relationships;
- Psychological responses to information: altered concept of self, feelings of depression, guilt and anger; and
- Detection of biological relationships within a family: paternity, maternity and adoption.

Currently, there is no state or federal regulation on whether or not individual subjects should be informed about test results or analyses performed on the subject, their biospecimens or data in the course of their participation in research studies. The purpose of this Policy is to establish how Incidental Findings made in research conducted by or under the auspices of NYU Langone Health should be handled and disclosed.

This Policy applies to all human subject research studies in which subjects can be identified and that could potentially generate results from research testing and/or procedures that are incidental to the primary research and could significantly affect the health of the subjects or their families. This includes but is not limited to research involving:

- Genetic testing of human biospecimens, such as tissue, blood, or saliva and/or collection of genetic information for research;
- Imaging such as MRI scans, CT scans, PET scans, X-rays and any other high density images that provide anatomic or physiological data of the type that is used for clinical diagnosis or treatment; and
- Other procedures for which there is some possibility as justified by the Principal Investigator that results or procedures could identify results or findings outside the aims of the research that would meet the criteria for the determination that individual research results should be returned to a study subject.

The Policy does not apply to research in which the subjects cannot be identified; i.e., (i) only de-identified data and results were collected and therefore the research is not human subjects research, and there is no code linking to identifiers available to the researchers, or (ii) the subject cannot otherwise be contacted. It also does not cover Incidental Findings on data and specimens that were collected and used solely for clinical purposes. The Policy applies only to data and specimens collected from identifiable subjects for primary research.

POLICY: GENERAL

Generally, results of tests and procedures performed on subjects solely for research purposes during the course of their participation in research should not be shared with study subjects. Results from such research procedures should only be returned to a subject as provided in the study's IRB-approved protocol and informed consent form.

Principal Investigators are not required to actively search for Incidental Findings. However, if an Incidental Finding is discovered about a research subject as a result of a research test or procedure and meets the criteria below, the Principal Investigator must report the Incidental Finding to the subject, unless the subject is

allowed to explicitly opt out of being informed of Incidental Findings through the study's informed consent form.

In order for Incidental Findings to be disclosed to a research subject, the following criteria must be met:

(1) The subject opted-in through the IRB-approved informed consent process to receive his/her individual results, unless the IRB has determined that an option to opt-out is not feasible (see *Opt-In/Opt-Out*, below).

(2) The IRB-approved research informed consent form states that Incidental Findings may be returned to the subject.

(3) The Incidental Finding is Analytically Valid or otherwise confirmed (for example, by follow-up imaging tests or by consultation with radiologist and physician); **AND** is either Clinically Significant **OR** Medically Actionable, as determined by a licensed physician.

Experts may be consulted to help the Principal Investigator determine whether the Incidental Finding is Clinically Significant or Medically Actionable.

Analytically Valid

Laboratory results: If an Incidental Finding was discovered through a research test result generated by a non-CLIA certified lab or non-diagnostic laboratory and is determined to be either Clinically Significant or Medically Actionable, the Principal Investigator should arrange for follow up testing to be done at a CLIA-certified clinical laboratory to validate the finding. Otherwise, the Principal Investigator must submit to the IRB an explanation of why clinical validation is not ethically appropriate or practicably possible. If there is no existing clinically accepted standard for validating the research result, the result should not be returned to the subject. Exceptions may be warranted if the Incidental Finding cannot be Analytically Validated but could be Clinically Significant or Medically Actionable. Any exceptions should first be discussed and approved by the IRB.

Imaging tests: If an Incidental Finding is revealed through a research imaging procedure, the Principal Investigator may need consultation with radiologist, patient's physician, and/or follow up procedure (such as of body parts other than that for which the research was performed) to confirm the finding.

(4) The IRB-approved disclosure plan, including the applicable terms of the research informed consent form, must comply with all applicable laws. For example: research studies that involve research genetic testing should include a way to ensure that the review and approval process is consistent with New York State law [Civil Rights Section 79-L] which applies to tests of human DNA, chromosomes, genes and gene products to learn whether an asymptomatic person is genetically predisposed.

Incidental Findings that do not meet all of the above criteria and are not approved for an exception by the IRB must not be disclosed to a research subject.

MEDICAL RECORD

If the subject will be notified of Incidental Findings, all Incidental Findings that will be reported to the subject must also be recorded in the medical record.

SUBMISSIONS TO THE IRB

For any study that possibly could generate Incidental Findings, the Principal Investigator must include in the protocol and IRB application a comprehensive plan for how Incidental Findings will be handled and when subjects will be informed. The study's informed consent form should also include statements on the possibility of Incidental Findings being discovered, and when and how results will be disclosed. The IRB may consider the plan to disclose Incidental Findings on a study wide or on a case by case (subject by subject) basis as appropriate.

IRB APPLICATION/PROTOCOL

In addition to other required elements, the IRB application should include the following:

- A plan for identifying and assessing which Incidental Findings are likely to be Clinically Significant or Medically Actionable. Because Incidental Findings may be outside the Principal Investigator's expertise, this could include a plan to obtain clinical expertise from licensed non-investigators as necessary (for example, a licensed radiologist for a study involving research imaging scans).
- Description of type of results that may be returned.
- Description of and qualifications of the individual(s) who will be responsible for disclosing the findings to the subject and how they are qualified/trained.
- Timing on when the Incidental Findings will be returned.
- How the Incidental Findings will be communicated.
- Plans for further care for the subject after Incidental Findings are discovered. This could include: follow-up testing to validate the result; pre- and post- genetic counseling for the subject; provision of care by the Principal Investigator; referral to another clinic, physician or provider; information about alternative resources for obtaining care.
- If the subject is a minor or an individual of diminished consent capacity, description of to whom the findings will be returned.
- Description of plans for allowing subjects to withdraw from the study, their specimens and inclusion of associated data in future analysis and reporting.
- Description of plans for sharing Incidental Findings with other investigators, if applicable.

COSTS

It is recommended that Principal Investigators include in the study budget the costs related to follow-up testing that may be required to validate Incidental Findings (e.g., laboratory costs for validation by a CLIA-certified lab, fees for genetic counseling). If funding is not obtained, such costs should be billed to the subject and/or the subject's insurer. The study's IRB application and informed consent form must explicitly address who will be responsible for these costs.

INFORMED CONSENT AND DOCUMENTATION PROCESS

Subjects should be informed of the potential for Incidental Findings being discovered before they are enrolled in the study through the IRB-approved research informed consent form.

The IRB-approved consent form must include the following:

- The choice to either opt-in or opt-out of being informed of Incidental Findings, unless an option to opt-out is not feasible as determined by the IRB. See *Opt-In/Opt-Out*, below.
- What type of results or Incidental Findings that may be returned to subjects (not a specific list of all results or findings), or if they will not be not returned, the reason why.

- An explicit statement that there is no guarantee that all Incidental Findings may be found through the research.
- Information on whether follow-up with a clinician is recommended for further testing.
- Whether and how the Incidental Findings will be reviewed to determine if they are appropriate to return.
- If Incidental Findings will be disclosed, description of how they will be shared (e.g., through genetic counseling).
- If Incidental Findings will be disclosed, explanation of forseeable risks and any benefits of making results or Incidental Findings available. Example: Incidental Findings that have uncertain clinical implications and where there are no known treatments or interventions may cause subjects undue concern, anxiety, and worry. Those that identify a major health problem could be of great benefit.
- If the study enrolls subjects who are minors, they must be provided the opportunity to consent to receive Incidental Findings and results when they reach the legal age of majority.
- If Incidental Findings will be disclosed based on the criteria established in this Policy and the subject has opted to be notified, subjects should be informed of the possibility that the results will be included in their medical record and therefore made available to any person or entity that becomes authorized to see a copy of their medical record, including potential employers and insurers.
- If follow-up testing will be required to validate the research test result before disclosure, subjects should be informed of who will be responsible for costs of such testing and for other costs related to follow-up, such as genetic counseling.

If applicable, the IRB may approve on a case by case basis a Principal Investigator's request to allow all study subjects to receive a form letter indicating that clinical testing is available and they may wish to have follow-up testing conducted at a certified clinical laboratory.

OPT-IN/OPT-OUT

The study's informed consent form must include language providing the subject the choice to explicitly either opt-in or opt-out of being informed of Incidental Findings. For studies using a radiology research procedure, opt-out language will not be required. Principal Investigators may bring any other requests for an exception to the IRB. The IRB, in conjunction with the Institutional Official, will decide whether the exception to exclude an opt-in/opt-out choice can be granted.

On a case by case basis, the Principal Investigator should consider whether the consent form should indicate that subjects will be contacted and offered a follow-up, or 'result-specific' consent process, in which the subject would be asked for confirmation that their initial opt-in/opt-out decision remains the same. If such follow-up is proposed, the Principal Investigator should include the plan in the IRB application for review.

DISCLOSURE PROCESS

Incidental Findings should first be assessed consistent with the plan outlined in the study protocol, and with consultation by an expert as necessary (such as a radiologist not on the study team). Incidental Findings may be disclosed to subjects only by a licensed physician, psychologist, genetic counselor, or other licensed professional as appropriate and consistent within the scope of the individual's licensure, through the IRB-approved disclosure process. *See IRB Application/Protocol*, above. Appropriately trained and supervised non-professional study personnel may communicate research test results with research subjects only with the IRB's approval.

Principal Investigators of studies that involve tests or measures that could possibly be expected to generate Incidental Findings requiring disclosure to research subjects should ensure results are de-identified while the test results are being analyzed, if the nature of the protocol does not contemplate collection of information and de-identification . Pending assessment of the Incidental Findings, a link to subjects' contact information should be retained. The information necessary to retain may include contact information and be kept linked to the tests until the results are known, after which time the link to contact information can be destroyed as appropriate. The Principal Investigator should retain a way to contact subjects until the outcome of the test is reasonably known. An exception to this requirement to retain subject contact information is applying tests to anonymous samples where subject identifiers were never known to the Principal Investigator.

If a research test in a study uncovers a potential Incidental Finding, the Principal Investigator should, before meeting with the subject, (1) determine the clinical implications of the result for the subject; (2) re-evaluate the subject's personal medical history, family history, and physical examination in light of the Incidental Finding, if appropriate; (3) review the subject's preferences communicated at the time of the research informed consent, e.g., did the subject opt out of receiving all or certain results; and (4) weigh potential harms and benefits of reporting the Incidental Finding.

The Principal Investigator should notify the subject that preliminary results indicate a confirmatory test is recommended and refer the subject for follow-up testing by their treating physician or other appropriate individual. In the case of genetic research, the Principal Investigator should notify the subject's physician of the need for possible further testing, and refer the subject to a genetic counselor as required by New York State law.

Subjects should also be informed that the costs of the follow-up testing, genetic counseling (if applicable), and treatment related to the Incidental Finding will be the subject's and/or their insurer's responsibility if not covered by the study's budget.

ADDITIONAL REQUIREMENTS FOR INCIDENTAL FINDINGS DISCOVERED IN GENETIC RESEARCH

The genetic counselor should guide the subject through a separate consent process to inform the subject that before specific results can be shared, they have the option to have the research test result confirmed through follow-up testing at a CLIA-certified laboratory, or that they can opt out of the follow-up testing and receiving further information. This separate consent process should provide the subject with information to enable the subject to decide whether they want to be provided with specific results. Other components of pre-test counseling should include:

- Explanation of the information that will/will not be returned
- Likelihood of detecting additional variants
- What the Incidental Findings could mean and how results could be used in the present and future.
- Gathering of the subject's family history not already known and discussion of risks that arise from the family's medical history
- Risks and benefits of learning of the specific Incidental Findings. Potential harms of disclosure of Incidental Findings after follow-up testing include: psychological distress from learning of disease risk, financial and personal costs of additional testing indicated, adverse consequences of therapeutic interventions for which evidence of benefit is lacking in patient who are diagnosed incidentally, possible legal ramifications of disclosure.

- Discussion of technical limitations of analysis for Incidental Findings (e.g., "false negative" results)
- Subject's current preferences for learning of the results from follow-up testing
- Discussion on whether the subject authorizes results and information to be shared with relatives and others if the subject becomes incapacitated or dies (post-mortem disclosure).

UNEXPECTEDLY IDENTIFIED INCIDENTAL FINDINGS

If the protocol does not include a potential need to share Incidental Findings, and an Incidental Finding that is Clinically Significant or Medically Actionable is unexpectedly identified, Principal Investigators should notify the IRB through a Reportable New Information (RNI) submission. This should be done by the Principal Investigator as soon as information that may impact an individual's health, safety or welfare is discovered in the course of the research. The Principal Investigator should include in the RNI submission (1) a recommendation on whether the Incidental Finding meets the criteria for disclosure to the subject; and (2) a disclosure plan which meets the requirements of what needs to be included in the IRB application as set forth above. The IRB must first approve disclosure of the information to the subject if the information or frequency was unanticipated in the approved protocol. *See also* IRB Policy, Section 8.8: Reportable New Information (reporting of Adverse Events).

18.11 INSTITUTIONAL POLICY ON RESEARCH WITH DIGITAL DATA COLLECTION TOOLS

DEFINITIONS

DIGITAL DATA COLLECTION TOOLS or ***DDCTS*** means software applications (**"APPS"**) or technologies on mobile or wirelessly communicating devices such as smartphones, free-standing monitors or sensors, or wearable devices that are used to collect, transmit, and/or disseminate private or non-private, actively or passively collected data or information on a research subject.

MCIT means NYU Langone Health's Medical Center Information Technology department.

POLICY BACKGROUND AND PURPOSE

Because of increased use of technology in healthcare and society in general, DDCTs are becoming increasingly common as a tool used to collect research data in human subjects research. In addition, some studies are specifically designed to develop, test, or validate the DDCTs themselves. The purpose of this Policy is to ensure that DDCTs that are used in human subjects research are used in a manner that protects the privacy of subjects. This Policy also seeks to ensure that the tools are compliant with NYU Langone Health's MCIT systems and data security requirements.

POLICY

All DDCTs that are being developed, tested, validated, or used to collect data in NYU Langone Health human subjects research are subject to NYU Langone Health's review and approval. These include DDCTs that are developed in-house and those provided by a research sponsor or other third party.

The origin of the DDCT (that is: whether it is a homegrown or commercially available product; sponsor or other third party-provided, free or licensed), the way in which the data will be used, and whether NYU Langone Health data will or will not be fed back into the product will affect the pathway to NYU Langone

Health's review and approval of the DDCT for use in the study and determine what other reviews are required before the DDCT can be used in the research.

Principal Investigators will be asked to indicate in the MyStudies/Research Navigator submission whether they plan to use a DDCT in their research to collect, transmit, and/or disseminate research subject data. MCIT Ancillary review may be required and the Principal Investigator will be notified through a notification in the system to complete an MCIT DDCT/Novel Technology form. When considering use of a DDCT, and before submitting a protocol that contemplates use of a DDCT, the product must first be reviewed by the Principal Investigator and research team. The study team's review must include review of any Terms of Service or End User Agreements associated with the DDCT. Review by the OSR Contracts team may also be required. Guidance on review of Terms of Service and End User Agreements can be found in *Human Research Protections-IRB Guidance, Research with Digital Data Collection Tools*.

SUBMISSIONS TO THE IRB

If a DDCT will be used in the research, the research protocol must include the following for the IRB's review:

- A description of the DDCT itself (e.g., what it is, is it home-grown or commercially available, who is providing it, how will it be used, who will use it);
- Type of data and list of each data element that will be collected/transmitted/disseminated;
- Whether or not data will be fed back into the DDCT;
- Summary of the Terms of Use and/or End User Agreement; and
- A data security plan, as further outlined below under *Data Security Plans, Incident Response and Mitigation*.

The IRB will review and approve use of the DDCT in the research only if it finds that adequate measures are in place to protect subjects' privacy and confidentiality.

The research informed consent form must include language that a DDCT will be used to collect, transmit, and/or disseminate (as applicable) information about the subject.

DATA SECURITY PLANS, INCIDENT RESPONSE AND MITIGATION

Research data collected through DDCTs is subject to the same data security principles that apply to human subject research data through other means. Researchers should consider whether data collected as part of the DDCT App function (e.g., location data) is necessary to the study and whether they should strip such data from the research data set.

For any research protocol that contemplates the use, development, validation, or testing of a DDCT, the Principal Investigator must include a data security plan that contains a review of the DDCT and whether considerations have been made to ensure that only the minimum necessary sensitive data is collected and stored. When sensitive data is collected or stored, the plan must indicate how researchers will protect the data and any copies or extracts of the data through its complete lifespan. The plan must also include provisions for the eventual destruction or de-identification of any sensitive data using industry best practices available at that time.

Additional information on pathways for review and approval of DDCTs, review considerations, and data security plans, incident response, and mitigation can be found in *Human Research Protections-IRB Guidance, Research with Digital Data Collection Tools*.

SURVEY TOOL TECHNOLOGY

A ***SURVEY TOOL*** is a technology that enables data to be collected directly from subjects through a series of questions included in the survey. Research data may be submitted by subjects through web-based Survey Tools (e.g., using the internet, a user can log-on to a site and fill out the survey) and/or externally-hosted online Survey Tools.

NYU Langone Health's MCIT currently permits the following Survey Tools to be used in research if the data collected WILL NOT include protected health information (PHI): Qualtrics, REDCap, and SurveyMonkey. If the data WILL include PHI, the only Survey Tool that is permitted for use is REDCap.

If any other Survey Tool is contemplated for a research study, investigators should first consult with MCIT. Before an IRB application or amendment is submitted that includes use of any Survey Tool that is not MCIT-approved or if the study contemplates use of the above Survey Tools in a way that is not MCIT-approved (e.g., PHI collected in a toll not approved for this use), MCIT must first evaluate the Survey Tool to ensure that it is acceptable and address the risks and technology considerations specific to such tools, as outlined below. All of this information should be used to create a data security plan submitted to the IRB as part of the research protocol.

MCIT's review will include looking at what data will be collected, who will submit the data through the tool, where the data is going, and whether there is any identifiable data that may be captured, i.e., whether the data collection form will present an opportunity for the individual entering data to enter PHI through open-ended questions.

1. **Security of sensitive information**: Whether there are information risks associated with use of technology that functions over a wireless network and through third-party platforms. Data transmitted over wire networks is susceptible to wiretapping or interception. The technology or website may keep track of the user's unrelated activities. When determining the risks to subjects' privacy and confidentiality, the sensitivity of the data being collected must be considered. It may be unacceptable to collect sensitive data online via internet/web-based Survey Tools without encryption or other methods that guarantee anonymity.

2. **Data ownership**: If a third party Survey Tool will be used, whether the terms of service provide that the third party may own some of the data and may also collect a variety of data that the company does not consider owned by the user. Companies often harvest sensitive data for advertising profiling.

3. **Data collection**: Whether the Survey Tool collects data manually or uses software (e.g., cookies and web beacons) to automatically collect data from users, and may be set to collect unintended data by the technology vendor. Depending on the survey design, identifiable data may be collected (e.g., Internet Protocol (IP) addresses, email addresses, etc.), allowing survey sites to trace survey response data back to individual responders.

4. **Data access**: Whether the Survey Tool may allow data to be accessed in different locations. If the data is collected on a personal device, additional risks should be considered (e.g., if the terms of agreement for the personal device were accepted under personal terms that did not contemplate the device would be used for research). Access rights should be defined for all folders and files in the physical storage media (e.g., only select research staff have the authority to modify backup files).

The data security plan included with the IRB submission should specify how subject identifiers will be protected, and how data stored on physical devices such as smartphones, hard drives, etc. will be protected from unauthorized access, use, loss, theft, or other violations of data use and protection terms.

5. **Data storage**: How data will be stored. Data should be stored on appropriate media (e.g., on the survey software, a software platform used to access the survey, Cloud services, or NYU Langone Health's server) to protect the sensitivity of the data, with appropriate role-based access.

6. **Data transmission**: How data will be transmitted. Data transmission refers to data in motion from one machine or device to another. Depending on the Survey Tool, the risk level of transmission may increase based on the method used to transfer data (e.g., wireless transfer intercepted by unauthorized parties) and if the Survey Tool software is not up to date. The data security plan should address how these risks of data interception will be mitigated.

7. **Data sharing**: Survey data and analysis can be shared within the survey platform with authorized users, by requesting the platform to email the survey data and reports by sending the data or sending a link to the data, or by saving the data to a server. The investigator should consider how to ensure that access to and sharing of the research data is sufficiently controlled.

8. **Data retention and destruction**: Depending on the Survey Tool, authorized users will be given read, write, edit, or delete access. Investigators should address how appropriate access will be given and removed, such as when research staff leave the institution. If data needs to be stored for a long period of time, the Survey Tool chosen should be assessed for long-term access for personnel monitoring and the form of media.

LIVE TWO-WAY COMMUNICATION TECHNOLOGY

LIVE TWO-WAY COMMUNICATION technology allows for simultaneous communication between two or more individuals through audio and visual communication channels. Commonly used forms of Live Two-Way Communication technology include telephone, instant messaging (e.g., text messaging, Google Chat, etc.), chat rooms (e.g., Discord), and video telephony or internet phone (e.g., FaceTime, Zoom, Skype, WebEx, using web cameras)**.** Instant messaging is a communication tool that allows users to send typed messages, pictures, files, and live video to one or more recipients. Chat rooms are similar to instant messaging but instead of one-to-one communication, users log into a virtual room or space to communicate with others in the "room." Video telephony or internet phone is a real-time, audio-visual communication tool. Live Two-Way Communication technologies use telecommunication networks established through public switch-enabled telephone wires, cellular networks, and other analog and digital technologies.

Investigators may use Live Two-Way Communication technology in their research if reviewed by MCIT, the IRB, and NYU Langone Health's Privacy Officer (as appropriate). NYU Langone Health currently permits only WebEx and Zoom to be used in research. If any other Live Two-Way Communication technology is contemplated, MCIT must first evaluate the technology. Use of text message is not an acceptable form of Live Two-Way Communication for communication with subjects in human subject research.

Before submitting an IRB application or amendment for research studies that include use of Live Two-Way Communication technology, investigators should consult with MCIT to ensure that the proposed technology is acceptable and address the following risks and technology considerations specific to such technology, as

outlined below. All of this information should be used to create a data security plan submitted to the IRB as part of the research protocol.

1. **Security of sensitive information:** Whether the confidentiality, integrity, and availability of data collected using Live Two-Way Communication technologies may be susceptible to threats. Risks associated with Live Two-Way Communication technologies can arise when the technology used to collect information is susceptible to wiretapping or interception of data, or when the technology or website keeps track of a user's unrelated activities. The data security plan should include details for how these risks will be mitigated and how security and access will be controlled.

   Live Two-Way Communication vendors may offer MCIT the ability to manage collaboration privileges and to enforce enterprise security policies. A policy, contract, or agreement may include prohibiting automatic recording or disclosures of identifiable information to third parties without authorization. Investigators should review these policies, contracts, or agreements and consider these concerns.

2. **Data ownership:** Whether the Live Two-Way Communication provider's terms of service provide that they or others may own some of the data and may also collect a variety of data that the company does not consider owned by the user. Live Two-Way Communication providers may impose terms of service that are not readily identifiable. For instance, these terms of service may unintentionally grant third parties access or intellectual property rights to data in violation of the communicating parties' expectations and data protection obligations. Terms of service should therefore be carefully reviewed.

3. **Data collection:** Whether the provider uses software that automatically collects data from users that the user does not intend to be collected. The vendor agreement should be carefully reviewed.

4. **Data access:** Whether the Live Two-Way Communication provider records communications or collects metadata such as time, location, address. If so, the user may not have the right to access the information collected by the company. The provider's policies should be reviewed to determine if this is the case.

5. **Data storage:** Whether the type of technology used, such as a smartphone, may be enabled to store or record Live Two-Way Communications. This poses the risk that information will be disclosed without authorization if the phone is lost or compromised. The data security plan should address whether there will be additional protections to address this risk.

6. **Data transmission:** Whether the Live Two-Way Communication technology may transmit data in different forms and uses transmission technologies such as internet protocols, cellular phone protocols, or public switches and routers. These channels may not be encrypted or secure. Investigators should consider these possibilities prior to choosing the technology used in their research.

7. **Data sharing:** Whether files and images can be shared through Live Two-Way Communication technologies over telephone wires, wi-fi, Bluetooth, and other data transmission technologies. These channels may not be encrypted or secure. Investigators should consider these possibilities prior to choosing the technology used in their research.

8. **Data retention and destruction:** Whether the Live Two-Way Communication technology provider can deny users the ability to retain or destroy data collected by the company. This concern should be addressed in contractual terms if possible.