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President and CEO

OPERATING PROCEDURE NO.: 180-9

**NYC HEALTH + HOSPITALS HUMAN SUBJECT RESEARCH PROTECTIONS
PROGRAM**

POLICIES AND PROCEDURES

TO: Senior Vice Presidents
Executive Directors
Medical Directors
Principal Investigators
Department Chiefs of Services
Chief Nurse Executives
Facility Research Review Chairs & Committees
Directors of Risk Management
Directors of Regulatory Affairs
Directors of Quality Management
Office of Corporate Compliance
Office of Legal Affairs
Chief Financial Officers
Facility Research Administration Offices
Office of Research Administration
Institutional Review Boards
Directors of Pharmacy

FROM: Mitchell Katz, MD

A handwritten signature in black ink, appearing to be "MK", written over the name Mitchell Katz.

DATE: January 17, 2019

RE: **Human Subject Research Protections Program Policies and Procedures**

This Operating Procedure, **NYC Health + Hospitals Human Subject Research Protections Program Policies and Procedures** replaces the **HHC Human Subject Research Protections Program Policies and Procedures** dated April 29, 2015.

This Operating Procedure has been revised to account for revisions made by the U.S. Department of Health and Human Services and fifteen other Federal Departments and Agencies to the Federal Policy for the Protection of Human Subjects (the "Common Rule"), on January 19, 2017, effective as of January 21, 2019.¹ The following changes have been made to the Common Rule and have been implemented in this revised Operating Procedure:

- Revisions to the definitions for the terms “human subject” and “research;”
- Elimination of the requirement for annual continuing review of certain categories of research, including research that is eligible for expedited review, is reviewed by the IRB in accordance with limited IRB review procedures, or has completed all interventions and is now limited to analyzing data or accessing follow-up clinical data from procedures that subjects undergo as part of clinical care;
- Elimination of the requirement for Institutional Review Boards (“IRB”) to review grant applications/funding proposals related to research;
- Addition of new categories of research exempt from IRB review, including research using benign behavioral interventions and storage or maintenance of identifiable data/biospecimens for secondary research for which board consent is required; and
- Revising the form and content of human subject informed consent documents.

Research initiated (i.e. initially approved by an IRB, or for which IRB review was waived or determined to be exempt) before January 21, 2019 will remain subject to the legal requirements of the prior version of the Common Rule (the “Pre-2018 Requirements”). Pre-2018 Requirements can be accessed using the following link: <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/regulatory-text/index.html#46.116>. All research, regardless of IRB approval or review date, will be subject to the administrative, institutional, and procedural requirements of this Operating Procedure. Questions regarding the applicability of or compliance with the Pre-2018 Requirements to a particular research project should be directed to the Office of Legal Affairs and the Office for Research Administration. Principal Investigators are encouraged to use best efforts to transition existing research to be subject to the revised Common Rule. Questions regarding how to transition existing research to the revised Common Rule should be directed to the applicable reviewing Institutional Review Board.

In addition to revisions required under the Common Rule, this Operating Procedure has been revised to reflect various updates and changes to state and federal laws and agency policies and guidance documents, as well as to account for institutional changes including updates to administrative requirements and a change of corporate name.

SCOPE: This Operating Procedure applies to all individuals involved with research conducted at H+H facilities, on behalf of H+H or that involve H+H patients, staff, or caregivers as research subjects.

EFFECTIVE DATE: January 21, 2019

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PREAMBLE¹

I. MISSION

NYC Health + Hospitals (hereinafter “H+H”) supports and promotes Research through fostering industry based or academic-community partnerships in which industrial and academic scientists and clinical researchers work together with community-based health care professionals and Research participants to better understand, detect, treat and prevent a wide range of diseases. All stakeholders utilize clinical, health services, community-based and translational research models, enabling them to make discoveries and/or advancements at the bio-medical level. Most discoveries are meant to be translated to the patient-centered clinical, health services and community level, enabling each of the H+H Facilities to promote and protect health in its fullest sense; the total physical, mental and social well-being of the people.

H+H protects Human Subjects’ rights and safety, and assures a regulatory and legally compliant environment for the conduct of ethical Research. This takes into account the unique sensitivities and vulnerabilities of the patients it serves. H+H will assist investigators and staff who conduct Research at H+H to be properly trained to develop and conduct Research and will facilitate the appropriate conduct of Research. H+H will also work with its Principal Investigators to facilitate the dissemination of results of the Research to all stakeholders, ultimately to achieve the overall mission to promote and protect, as innovator and advocate, the safety and health of New Yorkers.

II. PURPOSE

In an effort to encourage Research, the purpose of these H+H Human Subject Research Protections Program Policies and Procedures (hereinafter “Policies and Procedures”) is to provide guidance to members of the Research Team in complying with the ethical standards described in the Belmont Report: Ethical Principles & Guidelines for the Protection of Human Subjects of Research by the National Commission for the Protection of Human Subjects of Biomedical Research (1979) (the “Belmont Report”)² and applicable Federal, State, and local laws (including, where applicable, Tribal law passed by the official governing body of an American Indian or Alaskan Native tribe), and regulations that govern Research carried out, in whole or in part, at any of the Facilities of H+H or involving any H+H patients. These Policies and Procedures are also a statement of H+H’s principles and policies in regard to the rights and welfare of Human Subjects in the conduct of Research³. For clarification, the term “Research” includes research which uses H+H patients, Facilities, staff or resources or which is conducted, in whole or in part, at an H+H Facility; it only includes human research, (e.g. not animal studies). In order to protect Human Subjects and guide researchers, all individuals involved in Research at H+H must comply with these Policies and Procedures. Members of the Research Team who are employed by an Affiliate or other collaborating institution(s) shall also comply with that Affiliate’s or institution’s policies and procedures.

¹ Capitalized terms used but not otherwise defined in this Preamble are defined in Part I, Glossary of Commonly Used Terms.

III. SCOPE

A. To Whom These Policies and Procedures Apply.

These Policies and Procedures apply to all individuals involved with Research conducted at H+H Facilities or on behalf of H+H, or that involve H+H patients, staff, or caregivers.

B. Scope of Subject Matter.

These Policies and Procedures set forth requirements and recommendations with respect to the planning, development, implementation, and retention of information related to Human Subject Research at H+H, as well as financial aspects of such Research, such as billing. In addition, these Policies and Procedures provide guidance and establish requirements with respect to (i) policies and procedures and standards of conduct regarding Human Subject Research, (ii) establishing persons and departments within H+H responsible for operating and monitoring aspects of Human Subject Research under these Policies and Procedures, (iii) appropriate and regular education and training for individuals involved in Research, (iv) communicating and responding to allegations of improper/illegal activities or other systemic problem areas, (v) use of audits to assist in the reduction of identified problem areas, (vi) remedial measures with respect to research misconduct and financial conflicts of interest, and (vii) as discussed in United States Department of Health and Human Services (“DHHS”) guidance to hospitals and Public Health Service research awardees, taking corrective action where research misconduct, fraud, waste or abuse is detected in order to ensure that H+H’s commitment to detecting and deterring criminal conduct, fraud, waste and abuse in Human Subject Research is fulfilled.⁴

IV. ASSURANCE AND ETHICAL GUIDELINES

A. Assurance Program Requirements.

As required by the Federal government for institutions engaged in Human Subjects Research that is supported by any agency of DHHS, H+H has an approved assurance of compliance with DHHS regulations (45 C.F.R. § 46.103) for the protection of Human Subjects with the Federal Office for Human Research Protections (“OHRP”). This assurance is the Federal Wide Assurance (“FWA”).

H+H’s FWA (FWA-00009807) states that all of its activities related to Human Subject Research, regardless of funding source, will be guided by the ethical principles found in the Belmont Report, and will comply with the OHRP Terms of the Federalwide Assurance for Protection of Human Subjects for institutions within the United States, regulations set forth in 45 C.F.R. § 46 and all of its subparts (A, B, C, D) (the “Common Rule”), and all applicable Federal policies.

H+H will ensure that Institutional Review Boards (“IRBs”) designated under H+H’s FWA are approved by the New York State Department of Health (“NYSDOH”), to the extent required by law, and registered with OHRP⁵ as well as the Food and Drug Administration (“FDA”) where the IRB reviews clinical investigations regulated by the FDA.⁶ Further, H+H will ensure that, where any responsibilities are delegated to an IRB, an IRB Authorization Agreement is executed between H+H and the IRB. A current copy of H+H’s FWA will be maintained with the Human Protections Administrator and on the Research Administration Intranet website and thus will be readily available to each Facility at any time.

The Office of Research Administration will be responsible for the integrity of the FWA data on the website and will renew its FWA, as required under the regulations, every 5 years, even if no changes have occurred, in order to maintain an active FWA.

B. Ethical Guidelines.

H+H is committed to conducting Research with the highest regard for the welfare of Human Subjects. It upholds, and adheres to, the principles of The Belmont Report.

To satisfy this requirement, H+H has adopted the Belmont Report, attached hereto as **Exhibit 1**.

H+H engages only IRBs that are guided by the ethical principles established by the Belmont Report and partners with only those Principal Investigators and Sub-Investigators who fulfill these principles.

V. INTERACTION WITH OTHER POLICIES & AGREEMENTS

A. Other H+H Operating Procedures Superseded by these Policies and Procedures

These Policies and Procedures supersede any and all individual Facility or previous H+H policies related to Research except as set forth below.

B. Other H+H Operating Procedures Not Superseded by these Policies and Procedures

These Policies and Procedures do not supersede H+H Operating Procedure 240-23: HIPAA Clinical Investigation and Research Policy and Guidelines; H+H Operating Procedure 40-61: Time and Effort Reporting and Operating Procedure; H+H Operating Procedure 40-6: Grants, Trust, Donations, except to the extent monies are given to H+H for Research or to the extent any donations are of anatomical gifts. These documents should be read in tandem with this document, where applicable.

C. Policies and Procedures of Affiliates or Collaborating Institutions

H+H has given assurances to the Federal government that it will conduct Research in accordance with the Belmont Report and in compliance with Federal laws, regulations, policies and guidelines. For this reason, all members of the Research Team must comply with these Policies and Procedures, as well as the policies and procedures of any Affiliate or collaborating institution that is the Grantee for Research being conducted at H+H, unless any memorandum of understanding or other agreement between H+H and the Grantee directs otherwise. The policies and procedures of H+H and its Affiliates engaged in Research should generally be consistent with each other, as all such institutions have provided assurances to the Federal government with respect to protections of Human Subjects. To the extent that these Policies and Procedures conflict with those of an Affiliate or collaborating institution that is the Grantee, the Principal Investigator should seek from the Office of Research Administration written guidance with respect to his or her obligations under those conflicting policies and procedures.

D. **Administrative Services Agreements**

H+H may, from time to time, enter into agreements with other entities where it delegates authority to perform certain of the Office of Research Administration responsibilities detailed herein. Any such delegation will only be valid if made pursuant to a separate agreement (each, an “Administrative Services Agreement”) that has been reviewed and approved by the Office of Research Administration and the Office of Legal Affairs. Notwithstanding any provisions in an Administrative Services Agreement, H+H, through the Office of Research Administration and the Office of Legal Affairs, will retain ultimate authority over all operational and managerial decisions regarding H+H Facilities and the activities performed at Facilities.

VI. **ROLES & RESPONSIBLE PARTIES**

A. **H+H’s executive leadership** is responsible and accountable for:

1. The adoption of these Policies and Procedures;
2. The safety and quality of care of all H+H patients involved in Research at its Facilities; and
3. Providing access to an IRB that will approve any proposed Research by either providing such IRB internally or contracting with an external IRB. H+H will only designate on its FWA IRBs which are located in the United States, registered with OHRP and, if applicable, the FDA, and approved by the NYSDOH to the extent required by law.

B. **H+H’s Central Office, Division of Finance, Facility Finance Department, Facility Personnel and Administrators** are responsible for supporting and facilitating Research by complying with contractual requirements, facilitating systems and addressing issues raised by the Principal Investigator, members of the Research Team, or others in a timely manner. To the extent that travel and other expenditures are approved under a Grant or contract, the local Facility is to release funds for such expenditures in a timely manner with support, if needed, from the H+H Office of Research Administration.

C. The **H+H Research Council** serves as an expert advisory committee to H+H corporate administration that advises, advocates, promotes, supports and enhances the conduct of high quality clinical and health service research within H+H and by H+H investigators in collaboration with Affiliates and other research partners. Council membership is rotating and selected by the Office of Research Administration based upon expertise in the conduct of Research. The Research Council contains representatives from the various H+H Facilities and H+H Central Office, as well as other key stakeholders and experts who can foster development of Research within H+H.

1. The goals of the Research Council are:
 - a. To foster and strengthen internal and external partnerships and scientific collaborations to enable H+H to meaningfully participate in Research;

b. To develop a Research agenda for the corporation that would ensure that Research activities, projects, and programs are aligned with H+H's mission;

c. To promote systems thinking approach to identify existing barriers to Research within H+H and develop a strategic plan to address barriers and maximize resource utilization;

d. To utilize community engagement principles in conducting clinical trials and in disseminating results to the community.

2. In order to work towards its goals and accomplish its mission the Research Council will:

a. Elect a chair and vice-chair to lead and represent the Research Council. The Research Council will meet regularly, report to the H+H Chief Medical Officer and work closely with the Office of Research Administration. If needed, the Research Council may create subcommittees to focus on specific tasks.

b. Conduct a systematic review and evaluate existing projects, programs, and processes to identify barriers to the conduct of research, both centrally and locally, at H+H. The Research Council will also provide leadership in defining recommendations to address and overcome these barriers.

c. Participate in the development of a strategic plan to develop Research capacity and infrastructure at H+H Facilities, as well as H+H Central Office.

d. Monitor H+H's progress towards implementing H+H's Research agenda, monitor strengths, weaknesses and risks, and recommend resolution strategies.

e. Work with and review H+H Research systems to promote efficiencies and ensure that activities are completed in a timely fashion.

f. Review policy and procedures in the context of the new developments in Research regulations and advise H+H regarding updates.

g. Provide leadership in supporting novel science and safe application of scientific discoveries to the community.

D. The **Chief Medical Officer of H+H** has been appointed as the Signatory Official under H+H's FWA. In this role, the Chief Medical Officer is responsible for

1. Promoting a culture of conscience for the ethical conduct of Human Subject Research.

2. Authorizing any necessary administrative or legal action in connection with Human Subject Research.⁷

3. Reporting to the H+H Board of Directors and/or the Quality Assurance Committee of the Board periodically regarding Human Subject Research protection activities, audit results, investigations, findings, and other information with respect to identified risk areas, as further discussed in Subsection 15.2 of these Policies and Procedures.

4. In addition, the Chief Medical Officer is responsible for reporting to the H+H Board of Directors and H+H executive leadership on an annual basis the summary of Research performed at H+H compiled by the Office of Research Administration described in paragraph VI.F.4 of this Preamble.

E. The **Director of the Office of Research Administration** (“RA Director”) has been appointed as the Human Protections Administrator under H+H’s FWA. Consequently, the RA Director is the immediate Human Subject Research protection official with regard to Research. The RA Director is responsible for:

1. Serving under the FWA as the point of contact with OHRP and other Federal authorities for Human Subjects protection issues, including the investigation and reporting of non-compliance matters;

2. Playing a key role in ensuring that H+H fulfills its responsibilities under its FWA;

3. Setting standards for Human Subject Research education requirements;

4. Ensuring that all H+H personnel overseeing Research at H+H participate in and complete regular training with respect to Human Subject Research protections;

5. Ensuring that all IRBs utilized by H+H have entered into an IRB Authorization Agreement with H+H and overseeing those IRBs’ compliance with such agreements;

6. Receiving, investigating, and responding to Research-related complaints;

7. Responding to questions or concerns from Human Subjects or investigators; and

8. Overseeing adherence to these Policies and Procedures in accordance with the overall compliance effort set forth by the Office of Compliance, which may also monitor the Office of Research Administration’s oversight activities with respect to compliance with these Policies and Procedures.

F. The **Office of Research Administration** works in concert with the **Office of Legal Affairs** with respect to monitoring legal developments that may require revisions to these Policies and Procedures, as well as communicating any such changes to the H+H Research community. In addition, the Office of Research Administration has the following responsibilities:

1. *Education.* Leading educational efforts for Principal Investigators and their staff, researchers and research staff, and appropriate corporate officials, to:

- a. Guide research teams and administrators on completing human subjects protection training.
- b. Inform Facilities of important Research ethics and Human Subjects protection issues as they arise, including any legal or regulatory changes.
- c. Update manuals, forms and web-based information.
- d. Host seminars and lectures.
- e. Distribute literature.

2. *Advisory Role.*

- a. Provide counseling to Principal Investigators, researchers and all others as requested and needed.
- b. Visit Facilities regularly and meeting with Facility Research Coordinator, Facility Research Review Committee, Principal Investigators, Research staff and grants officers.

3. *Compliance and Oversight.*

- a. Oversee the compliance of any ongoing Research involving Human Subjects with Federal, State and Corporate regulations and report any problems or concerns to the Office of Legal Affairs, Office of Corporate Compliance, and Facility Executive Directors and/or Medical Directors, and OHRP, as required.
- b. Oversee H+H compliance with Federal and State regulations regarding protection of Human Subjects and report any problems or concerns to the Office of Legal Affairs, Office of Corporate Compliance, and Facility Executive Directors and/or Medical Directors, and OHRP, as required.
- c. Research and select IRBs for H+H; and review the IRB Policies and Procedures for compliance with Federal and State requirements.
- d. Perform audits and quality assurance activities as required by Section 15.

4. *Reporting to H+H Board of Directors and Corporate Leadership.* The Office of Research Administration will be responsible for compiling a summary of the scope and type of Research performed at H+H to be presented to the Chief Medical Office on a monthly basis.

G. The **Principal Investigator** is the individual responsible for protecting the rights and welfare of Human Subjects and for the carrying out of sound ethical Research consistent with protocols approved by the IRB and H+H and the overall conduct of the Research. The Principal Investigator must ensure that all Research is conducted in an ethical manner and in accordance with all Federal, State, and local laws and regulations, institutional policies, and requirements or

determinations of the IRB. The Principal Investigator has the ultimate responsibility for the overall conduct of a Research Project, including all technical, programmatic, financial, compliance and administrative aspects. The responsibilities of the Principal Investigator are:

1. Supervising the conduct of Research Projects.

The Principal Investigator may delegate Research Project-related tasks, but must adequately supervise Research personnel to whom tasks are delegated. When supervising the conduct of Research, the Principal Investigator must ensure that:

- a. Research personnel are qualified by training and experience to perform Research Project-related tasks that have been delegated to them;
- b. Research personnel have an adequate understanding of the Research; and
- c. Research personnel follow the Research Protocol, including the recruitment, consenting, data collection, IRB reporting and other protocol activities.

2. Protecting the rights, safety, and welfare of Human Subjects.

The Principal Investigator or other qualified individual(s) must be available to provide Human Subjects with reasonable medical care for any medical problems that arise during participation in the Research Project that are, or could be, related to the Research Project. Additionally, when participation in the Research Project might impact the Human Subject's health and/or medical care, the Principal Investigator should attempt to inform the Human Subject's primary care physician, if medically appropriate, about the Human Subject's participation in the Research Project if the Human Subject has identified a primary care physician.

When protecting the rights, safety, and welfare of Human Subjects, the Principal Investigator's (or his/her delegate's) responsibilities include obtaining valid Informed Consents prior to commencing Research;⁸ adhering to IRB requirements and applicable law with respect to progress reports, continuing review and approvals; reporting to the IRB any unanticipated problems involving risks to subjects or others;⁹ maintaining records as required by these Policies and Procedures and applicable law; ensuring that drugs, biological products, and devices being investigated or used are managed and controlled as required by these Policies and Procedures and applicable law; following Facility, H+H and sponsor close-out procedures upon completion of the Research Project; and, if requested, making Research records available to H+H, the Sponsor/Grantor and governmental agencies for oversight of the Research Project.

H. All **Research Team** members:

1. Are expected to be familiar with the requirements of the Common Rule¹⁰ and other Federal laws and regulations, applicable State and local law governing the

conduct of Research, H+H policies and procedures, including these Policies and Procedures, the terms and conditions of any Research agreements with Sponsors and Grantors, and the basic ethical principles that guide Research; and

2. Shall, in the event that they have any questions or are unfamiliar with H+H policies and procedures and relevant law governing Research, seek advice from the Office of Research Administration, Facility Research Coordinator, Principal Investigator, IRB or Sponsor or Grantor, as applicable; and

3. Must complete any training required by H+H, the relevant IRB, and other review units prior to initiating a Research Project. Research Team members should not undertake responsibility for Research Projects unless they understand these requirements and can comply with the relevant standards for protecting the rights and welfare of Human Subjects.

I. The Executive Director, Medical Director, or Director of Pharmacy, as applicable, of each Facility is responsible for:

1. Ensuring that the Pharmacy Department and relevant staff are made aware of and trained on these Policies and Procedures on an ongoing basis;

2. Ensuring compliance with these Policies and Procedures (see **Exhibit 2**, Facility Commitment Form); and

3. Ensuring facilitated systems to comply with contractual agreements related to Research.

J. The Medical Director and Chief Nurse Executive, as applicable, of each Facility is responsible for:

1. Ensuring that the Department Chiefs of Services and relevant medical and nursing staffs are made aware of and trained on the Policies and Procedures on an ongoing basis;

2. Instituting necessary corrective actions for each department or individual medical provider;

3. The day-to-day compliance of the medical and nursing staffs with these Policies and Procedures (see **Exhibit 2**, Facility Commitment Form).

K. The Facility Research Review Committee is responsible for:

1. Ensuring that protocols and related activities are compliant with the operating procedures of H+H and the relevant Facility; and

2. Operational, clinical and fiscal feasibility.

L. Each Facility is accountable for the safety and quality of care, treatment and services provided at such Facility.¹¹ Therefore, each Facility is responsible for the implementation

of these Policies and Procedures, as certified according to the Facility Commitment Form set forth in **Exhibit 2**.

VII. INTERPRETATION AND COMPLIANCE

A. Interpretation of These Policies and Procedures.

In the event that a question arises as to the applicability or interpretation of these Policies and Procedures, the Office of Research Administration will make such determinations centrally, in consultation with the Office of Legal Affairs and, as needed, the Chief Medical Officer, Principal Investigator(s), Office of Corporate Compliance and the Facility Research Coordinator. The Office of Research Administration will communicate such determinations to the applicable IRB, all Principal Investigators, and related Research staff.

B. Compliance with Law, Regulations and Policies

H+H shall ensure that all Research is conducted in compliance with applicable Federal, New York State and local laws (including, where applicable, Tribal law passed by the official governing body of an American Indian or Alaskan Native tribe), regulations, and guidelines, including but not limited to, those listed in **Exhibit 3**.

VIII. PROCEDURE FOR UTILIZATION OF PROCEDURES AND FORMS

These Policies and Procedures, including the attached documents and forms, shall be available for reference to all H+H staff and anyone else conducting Research.

PART I

GLOSSARY OF COMMONLY USED TERMS

For purposes of these Policies and Procedures, the following definitions shall apply:

“Affiliate” means an institution, physician practice or other entity with which H+H has entered into an Affiliation Agreement which contemplates a relationship that involves Research activities and/or patient care.

“Chief Medical Officer” or **“CMO”** means the Chief Medical Officer of H+H.

“Chief Nurse Executive” means the chief nursing officer of H+H.

The **“Common Rule”** means the Federal Policy for the Protection of Human Subjects found at 45 C.F.R. Part 46.

“DHHS” means the U.S. Department of Health and Human Services.

“Executive Director” means the person then serving as the executive director of a Facility.

“Facility” means a facility owned and operated by H+H.

“FDA” means the U.S. Food and Drug Administration.

“Federalwide Assurance” or **“FWA”** means the federally required assurances described in paragraph IV.A of the Preamble of these Policies and Procedures.

“FRC” means the Facility Research Coordinator who is appointed by Facility leadership.

“FRRC” means the Facility Research Review Committee of the Facility whose members may include representatives of the Facility’s program offices, the Facility’s Division of Finance, and the Corporation’s Office of Legal Affairs, all of whom have received the approval of the Executive Director and the Corporation to become such a member.

“Grant” means, in general terms, financial assistance given to H+H by the Federal or State Government, or from a Sponsor, for a specific purpose to support instruction, research, or health or other public service. For the purposes of these Policies and Procedures, the term “Grant” includes financial assistance H+H receives indirectly from the Federal or State Government, or from a Sponsor, in the form of a sub-award.

“Grantee” means the entity that receives funding from the Sponsor or Grantor to conduct Research.

“Grantor” means a governmental entity, including a Federal, State or local government agency that provides funding for a Research Project.

“H+H” means NYC Health + Hospitals.

“Human Protections Administrator” means the Director of the H+H Office of Research Administration.

“Human Subject” shall have the same meaning as the definition of Human Subject under any of the following laws and/ or regulations (each as may be amended from time to time), regardless of whether direct patient care services are rendered to the individual.

45 C.F.R. Part 46

“A living individual about whom an investigator (whether professional or student) conducting Research: (1) obtains information or biospecimens through intervention or interaction with the individual and uses, studies, or analyzes the information or biospecimens; or (ii) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.”¹²

21 C.F.R. §50.3(g)

“An individual who is or becomes a participant in Research, either as a recipient of a Test Article or as a control.”

New York State Public Health Law Article 24-A

“Any individual who may be exposed to the possibility of injury, including physical, psychological or social injury, as a consequence of participation as a subject in any Research, development, or related activity which departs from the application of those established and accepted methods necessary to meet his needs or which increases the ordinary risk of daily life including the recognized risks inherent in a chosen occupation or field of service.”

The term “Human Subject” includes an individual whose tissue is used in Research and who may be individually identifiable by a Principal Investigator or the Principal Investigator’s staff. If at any time such individual receives direct patient care services, he or she shall also be considered a patient for purposes of this Policy.

“Informed Consent” means the consent of a Human Subject that contains the elements pursuant to 45 C.F.R. 46.116, 21 C.F.R. 50.25 and New York Public Health Law Article 24-A, as applicable.¹³

“Institutional Review Board” or **“IRB”** means an institutional review board established in accordance with and to carry out the purposes of 45 C.F.R. Part 46, 21 C.F.R Part 56, and New York Public Health Law § 2444.

“Invention” means any discovery or invention (whether or not patentable) created, conceived or reduced to practice as a result of Research including, but not limited to, all copyright and copyrightable material (unless published in academic or scholarly media or otherwise in the public domain), and all such intellectual property rights inhering in tangible research property.

“Medical Staff” means the body of persons comprised of licensed physicians and other licensed persons specified in the Medical Staff By-Laws of the Facility who are permitted by law and by H+H to provide direct patient care services to patients, that is organized pursuant to, and has responsibilities as are set forth in applicable laws and regulations, and that has the overall responsibility for (i) the quality of the professional services provided by persons with clinical privileges who provide direct patient care services to patients at the Facility and (ii) the accounting therefore to the Facility executive leadership.

“Medical Staff By-Laws” means by-laws that prescribe the organization, roles and responsibilities of the Medical Staff of the Facility, adopted and periodically reviewed by the Medical Staff of the Facility and approved by the Facility executive leadership.

“NIH” means the DHHS National Institutes of Health.

“NYSDOH” means the New York State Department of Health.

“Office of Legal Affairs” means the Office of Legal Affairs of H+H.

“Office of Research Administration” means Office of Research Administration of H+H.

“OHRP” means the HHS Office of Human Research Protections.

“Principal Investigator” means the individual who i) is qualified under Part II, Section 1 of these Policies and Procedures; ii) is responsible for overseeing a Research Project conducted at a Facility; and iii) has responsibility for the overall conduct of a Research Project.¹⁴

“RA Director” means the director of the Office of Research Administration.

“Research” means an activity that meets any of the definitions of research stated in any of the following laws and/or regulation (each as may be amended from time to time) and which uses H+H patients, facilities, staff, or resources or which is conducted at a Facility:

DHHS Regulations

“A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.”¹⁵

FDA Regulations

“Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or need not meet the 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 later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.”¹⁶

New York Public Health Law Article 24-A

“Any medical experiments, research, or scientific or psychological investigation, which utilizes human subjects and which involves physical or psychological intervention by the researcher upon the body of the subject and which is not required for the purposes of obtaining information for the diagnosis, prevention, or treatment of disease or the assessment of medical condition for the direct benefit of the Human Subject. Human research shall not, however, be construed to mean the conduct of biological studies exclusively utilizing tissue or fluids after their removal or withdrawal from a human subject in the course of standard medical practice, or to include epidemiological investigations.”

“Research Authorization Form” means the document through which a Human Subject gives his or her authorization for the use and disclosure of personally identifiable health information and which meets the criteria set forth in H+H HIPAA Clinical Investigation and Research Policy and Guidelines, at Section 2.1.

“Research Council” means the body of H+H Facility representatives that serves as an expert advisory committee to H+H and provides advocacy for Research activities.

“Research Project” means the specific Research Protocol: (1) for which funding has been or will be given by a Sponsor or Grantor and into which Human Subjects are actually or anticipated to be enrolled or (2) for which there is no funding and that is undertaken by a student as part of educational requirements or by a Principal Investigator undertaking a prospective chart review, retrospective chart review or informational review.

“Research Team” means Principal Investigators, any Sub- or co-investigators, Facility Research Coordinators and other staff who contribute to the scientific development or execution of a Research Project in a substantive, measurable way.

“Sponsor” means a private, non-governmental entity which provides funding for a Research Project.

“Sub-Investigator” means anyone other than the Principal Investigator who is involved in conducting Research or is responsible for the design, conduct, or reporting of Research.

PART II

PRELIMINARY CONSIDERATIONS FOR COMMENCING RESEARCH AT H+H

SECTION 1. ELIGIBILITY TO CONDUCT RESEARCH

1.1 Policy

A Principal Investigator may be whomever is most appropriate to carry out the Research Project including, but not limited to, a physician, nurse, social worker, student and/or other clinical staff, as outlined below:

1.1.1 Physicians. A physician may act as Principal Investigator for a Research Project if he or she is:

- (a) A person licensed under Title VIII of the New York State Education Law to perform diagnosis, treatment, medical services, prescription or therapeutic exercises with regard to or upon human beings;
- (b) A full-time, part-time and voluntary physician who is a member of the Medical Staff at the Facility at which the Research is to be conducted;
- (c) Has appropriate clinical privileges as defined in the Facility's Medical Staff Bylaws; and
- (d) Has the approval of their director of service or the chair of his or her department.

1.1.2 Other non-physician, clinical staff. Other non-physician, nurse or clinical staff may act as Principal Investigator for a Research Project if he or she has been previously authorized through the Facility's Medical Staff Bylaws or any other clinical or credentialing process of the Facility in which the Research is to be conducted. All such clinical staff will comply with any applicable requirements relating to the conduct of Research set forth in law or regulations established by the New York State Department of Education, Office of the Professions.¹⁷

1.1.3 Students. "Students", which includes any individual in training, such as residents and fellows, must comply with the policies of the reviewing IRB regarding students, mentorship, faculty involvement and/or any other oversight.

1.1.4 IRB Discretion. It should be noted that another entity reviewing a Research Project may have its own policies regarding who can be the Principal Investigator on a Research Project. Some IRBs are strict in this allowance, while others allow any person deemed competent and qualified to lead a Research Project. For cases in which an individual may not be eligible to be a Principal Investigator under the policies of a specific IRB, such individual may: (1) find another IRB which does allow for him/her to function in this role or, (2) such individual may follow that IRB's policies and find a co-investigator that does satisfy the requirements.

1.2 Procedure.

No additional procedure, outside of what has been identified above.

SECTION 2. DEFINING HUMAN SUBJECT RESEARCH AND EXEMPT RESEARCH DETERMINATIONS

2.1 Policy.

No Research involving Human Subjects may be conducted at H+H without IRB review and approval or an IRB determination of exempt-status. Determination as to whether or not a given Research Project meets the definition of Human Subject Research may be made by the Office of Research Administration, while determinations as to whether a given Research Project is exempt from IRB review must be made by an IRB in accordance with the procedures outlined below.

2.2 Procedure.

2.2.1 Human Subject Research Determinations. The Office of Research Administration may determine whether or not a given Research Project meets the definition of Human Subject Research and is therefore subject to IRB review and approval. Principal Investigators must, upon request, provide the Office of Research Administration with all information necessary to make such a determination. The Office of Research Administration will notify the Principal Investigator when a determination is made.

In order to determine whether an activity meets the definition of Human Subject Research, the Office of Research Administration must determine: (a) whether the activity in question meets the definition of Research and, if so, (b) whether the Research involves Human Subjects.

(a) An activity will meet the definition of Research if it is a systematic investigation designed to develop or contribute to generalizable knowledge¹⁸;

(b) Research involves Human Subjects if the Principal Investigator obtains data about a living individual through intervention or interaction or identifiable private information. "Intervention" includes both physical procedures by which data are gathered and manipulations of the Human Subject or the Human Subject's environment that are performed for Research purposes. "Interaction" includes communication or interpersonal contact between Research Team members and Human Subjects. 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. "Private information" must be individually identifiable, meaning that the identity of the Human Subject is or may readily be ascertained by the Principal Investigator or associated with the information, in order for obtaining the information to constitute Research involving Human Subjects.¹⁹

2.2.2 Exempt Research Determinations. Determinations as to whether a Research Project is exempt from IRB review must be made by a reviewing IRB. A Principal Investigator who believes a given Research Project is exempt from IRB review should submit a request to the IRB for an exemption determination. A Research Project may be exempt from IRB review in the following circumstances²⁰:

(a) The Research is conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) Research on regular and special education instructional strategies; or (ii) Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(b) The Research involves the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior, unless: (i) information obtained is recorded in such a manner that Human Subjects can be identified, directly or through identifiers linked to the Human Subjects; and (ii) any disclosure of the Human Subject's responses outside the Research could reasonably place the Human Subjects at risk of criminal or civil liability or be damaging to the Human Subject's financial standing, employability, or reputation.

(i) Research that involves the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not otherwise exempt from IRB review will be eligible for an exemption if (i) the Human Subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information be maintained throughout the Research and thereafter.

(c) The Research involves the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, and these sources are either publically available or if the information is recorded by the Principal Investigator in such a manner that Human Subjects cannot be identified, directly or through identifiers linked to the Human Subjects.

(d) The Research is conducted by or subject to the approval of department or agency heads, and is designed to study, evaluate, or otherwise examine: (i) public benefit service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

(e) Taste and food quality programs and consumer acceptance studies if (i) wholesome foods without additives are consumed; or (ii) 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 Services of the U.S. Department of Agriculture.

DHHS retains final authority as to whether a particular Human Subject Research Study is exempt.

2.2.3 Ethical considerations for Exempt Studies. Research Projects may be deemed exempt by the IRB if: (1) the research is exempt under 45 C.F.R. § 46.104(d); (2) the IRB finds and documents that informed consent can be waived (45 C.F.R. § 46.116(e) or (f)); or (3) the IRB finds and documents that the Research meets the requirements of the HHS Secretarial waiver under 45 C.F.R. § 46.101(i) that permits a waiver of the general requirements for obtaining informed consent.²¹ Regardless of exemption status, all Research Projects that involve the use of protected health information remain subject to the Health Insurance Portability and Accountability Act of 1996 (HIPAA; Pub.L. 104-191, 110 Stat. 1936). Principal Investigators should include a HIPAA Authorization or a request for a waiver of HIPAA Authorization in the exemption request submitted to the IRB if protected health information will be collected under the Research Project.

2.2.4 FDA-Regulated Research. Research Projects involving any Test Article (as defined in Section 17.2) or Biological Product (as defined in 16.1.2) must be submitted to an IRB for a determination as to whether the Research Project meets the definition of Research under the FDA regulations.

SECTION 3. TRAINING OF RESEARCH TEAM, REVIEWERS AND OTHERS.

3.1 Policy.

Federal and State regulations and guidelines require documented evidence that Principal Investigators, co-investigators, collaborators, study RA Directors and/or other individuals involved in Human Subject Research are qualified and have the expertise needed to protect Human Subjects. To meet this requirement and H+H ethical standards, H+H requires all individuals eligible to participate in carrying out a Research Project or conducting Research in any way at a Facility to participate in and complete training on Human Subject protections.

3.2 Procedure.

3.2.1 Research Team Training.

(a) *Initial training.* Prior to their involvement in Human Subject Research and before commencing Research at H+H for the first time, the Research Team must participate in and complete selected modules of the Collaborative Institutional Training Initiative (CITI) Course in the Protection of Human Research Subjects, as determined by the Office of Research Administration, which may include various modules on Human Subject protection, the Belmont Report, these Policies and Procedures, and others.

(b) *Continuing training.* After meeting initial educational requirements, members of the Research Team are required to meet a continuing education requirement every three years. Continuing education requirements may

be met either by completing a CITI refresher course or other training required or approved by the Office of Research Administration.

(c) *Additional Training.* In addition to H+H's required training as described above, the Research Team is required to satisfy any initial and continuing Human Subject protection training and education required by his or her respective IRB or Facility's medical staff bylaws.

3.2.2 FRRC Training. In order to be eligible to sit on the Facility Research Review Committee, members must participate in and complete selected modules of training offered by the DHHS's National Institute of Health ("NIH"), as determined by the Office of Research Administration.

3.2.3 Training for Other Research Personnel. Others who are involved in the review of Research at H+H, such as the Facility Research Coordinator and Facility Executive Directors, must participate in and complete selected modules of training offered by the DHHS's NIH, as determined and deemed necessary by the Office of Research Administration.

SECTION 4. H+H RESEARCH APPROVAL PROCESS

4.1 Policy.

In order to ensure that researchers comply with Federal, State, City and Corporate policies and regulations that guide Human Subjects Research at H+H, all Research Projects must undergo the approval process described herein.

H+H approval will not be granted unless an IRB determination as to the type of review required for the Research Project (Full Board, Expedited or Exempt) has been made. After review and approval or determination of Exempt status, as applicable, by the designated IRB, Research Projects will be reviewed by the FRRC, then H+H Facility executive officers and lastly, the Office of Research Administration.

Please see **Exhibit 4** for the Research Project Approval Process Map.

4.2 Procedures.

4.2.1 STEP I: Pre-Approval of the Research Project. This phase is to determine a Research Project's operational and financial practicability at H+H. Before submitting a Research application for funding from a Grantor or a Sponsor, whether or not in collaboration with another institution, department or colleague, the Principal Investigator must have a feasibility consult with the FRC of the impacted Facility(ies) to confirm that the Research Project can be accommodated by the implicated departments and individuals at the Facility and that sufficient funds will be requested from the Grantor or Sponsor for the conduct of the Research Project at H+H or using H+H patients. This Step I must be complied with by any Principal Investigator where H+H will be a grantee or subgrantee under any funding received from a Grantor or Sponsor or for any other Research Project where H+H Facilities or patients will be used or will participate. The FRC can involve as many expert reviewers as needed, and the Principal Investigator may

request that the Facility's Executive Director or Medical Director be included in the feasibility review.

(a) *Multi-Facility Research Projects.* Where a Principal Investigator intends to conduct Research at multiple H+H Facilities, the Principal Investigator must contact the Office of Research Administration to facilitate pre-approval. In addition, a Facility, Principal Investigator must be identified for each Facility participating in the Research Project.

(b) *Multi-Site Research Projects.* Where the Research Project is to be part of a multi-site Research Project that will rely on a single IRB, the Principal Investigator must identify the single IRB of record so that the Office of Research Administration can evaluate if an appropriate IRB Authorization Agreement is in place with the identified single IRB.

(i) *Multi-Site Research Projects funded by the NIH.* Consistent with the NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research ("NIH Single IRB Policy"), H+H requires the use of a single IRB of record for all non-exempt Research Projects funded by the NIH that are carried out at more than one site in the United States. A Principal Investigator who wishes to submit an application for funding to the NIH for a multi-site Research Project must first submit a plan for the use of a single IRB to the Office of Research Administration. The plan must include a statement confirming that participating sites will adhere to the NIH Single IRB Policy and must describe how communication between sites and the single IRB will be handled. Upon approval from the Office of Research Administration, the Principal Investigator may submit this plan to the applicable NIH Institute/Center.²²

(1) If, in delayed-onset Research, a single IRB has not yet been identified at the time the Principal Investigator intends to submit an application for funding for a multi-site Research Project to the NIH, the Principal Investigator must submit a written certification to the Office of Research Administration stating that he or she will follow the NIH Single IRB Policy and will obtain Office of Research Administration approval of the single IRB before initiating the multi-site Research Project. The Principal Investigator may submit his or her application for funding to the applicable NIH Institute/Center immediately thereafter.

(c) *Collaborative Research Projects with Affiliates.*

(i) *Designation of Facility Principal Investigator.* Before any Research Project can be undertaken with an Affiliate, an H+H Principal Investigator must be designated at the Facility(ies) at which the Research Project will take place. The designation of the H+H Principal Investigator must be on record with the Office of Research Administration before conduct of the Research Project can begin at the Facility(ies). Upon written

request, the Office of Research Administration may waive this requirement if, after review and consideration, it determines the Research Project in question does not require the designation of an H+H Principal Investigator at the Facility(ies). Affiliates are required to provide the Office of Research Administration with all information and documentation it requests in order to make such a waiver determination.

(ii) *Affiliate Policies and Procedures.* Principal Investigator(s) from Affiliate institutions must also consult with the appropriate offices within the Affiliate if required by such Affiliate's policies regarding collaborative research.

4.2.2 STEP II: IRB and Contract/Agreement Negotiations.

(a) *IRB Submission.* If an appropriate IRB Authorization Agreement is in place with the reviewing IRB, please complete an IRB submission as directed by the IRB.

(b) *IRB Review of Submission.* The IRB will review the Research Protocol and consent forms and/or relating documents for the scientific soundness of the Research Project, risks, benefits and any ethical issues relating to the safety and general welfare of the Human Subject. (Please see Section 5 of these Policies and Procedures regarding Informed Consent, and H+H HIPAA Clinical Investigation and Research Policy and Guidelines, at Section 3.1 and 3.3 for more information regarding the criteria and procedure for applications for waivers of HIPAA authorization requirements.) The IRB will transmit an IRB determination directly to the Principal Investigator.

(c) *Contract/Agreement Negotiations.*

(i) All Research-related contracts must be sent to the Office of Research Administration for review and the Office of Legal Affairs for final approval before being executed. The Office of Research Administration will review and negotiate the terms and conditions of the agreement in consultation with the Principal Investigator and other H+H departments, including the Office of Legal Affairs.

(ii) Once the Office of Research Administration has finalized the contract, it will be forwarded to the Office of Legal Affairs for final review and approval. The Office of Research Administration will notify the Principal Investigator and FRC once the contract has been approved and provide a copy of the final contract to the Principal Investigator.

(iii) The CMO, or appointed designee, is authorized and is required to sign on behalf of H+H all Research agreements with a Sponsor, Grantor, or collaborator that have been reviewed by the Office of Research Administration and approved by the Office of Legal Affairs as set forth above.

(iv) Once the Office of Research Administration has finalized the contract, the Office of Research Administration will notify the Principal Investigator and FRC when the contract has been approved and provide a copy of the final contract to the Principal Investigator.

(v) The provisions required to be included in Research agreements are listed in **Exhibit 5**. However, Principal Investigators should not rely on this information as a substitute for obtaining review by the Office of Research Administration and approval by the Office of Legal Affairs.

4.2.3 STEP III: Facility Review and Approval Process.

(i) STAR. In order to obtain H+H approval, the Principal Investigator must submit an application for the Research Project by uploading required information directly into the electronic submission system, which is the System to Track and Approve Research (STAR). Facility will not duplicate the review conducted by the IRB.

(ii) Completed Application. The FRC will conduct a preliminary review for completeness before forwarding the application to selected members of the FRRC. If the FRC determines an application is incomplete, the FRC will promptly communicate such findings to the Principal Investigator and work with the Principal Investigator for appropriate action. A completed application will include:

- (1) The Research Protocol,
- (2) The IRB determination letter,
- (3) Any Informed Consent/waivers/alterations, and HIPAA Research Authorization Form and/or waivers thereof,
- (4) Any applicable contract with the Grantor or Sponsor, if executed;
- (5) Any applicable approved budget;
- (6) Comprehensive Billing Plan in accordance with Section 31.3 of these Policies and Procedures or Medicare Cost Analysis, if applicable, under Section 33.3.2 of these Policies and Procedures for the Research Project.

(iii) FRRC Review. After the FRC certifies completeness, the application is forwarded to the FRRC through STAR in a timely manner. If the FRRC cannot approve the Research Project as submitted by the Principal Investigator, it will promptly communicate such findings to the Principal Investigator. (Please see H+H HIPAA Clinical Investigation and Research Policy and Guidelines, at Section 3.0 for more information

regarding IRB or Privacy Board considerations in connection with applications for waivers of HIPAA authorization requirements.) Where Affiliate is the Grantee and no agreement between H+H and the Affiliate describes how Research Project Costs (as that term is defined in Section 31.2 of these Policies and Procedures) are to be calculated and paid to H+H, the FRRC may not approve the proposed Research Project until H+H and Affiliate have agreed in writing how such costs will be reimbursed to H+H with respect to such proposed Research Project and such agreement has been approved by the Office of Legal Affairs.

(iv) Facility Executive Review and Approval. If the FRRC approves a Research Project, the completed application will be automatically forwarded to the medical director or medical board president, and the Executive Director of the Facility for review and approval. Upon approval by the Facility executives, STAR will automatically forward the application to the Office of Research Administration.

In the event that the Executive Director does not approve a Research Project, a summary statement should be sent on a timely basis to the Principal Investigator, who may then discuss the decision with the Executive Director. If the Principal Investigator and Executive Director cannot reach an agreement, the Principal Investigator may appeal the decision to the Office of Research Administration.

(v) Delegates and Alternates; Identifying a Designee. An FRRC or Executive reviewer may identify a designee in STAR to review and approve a completed application on his/her behalf.

4.2.4 STEP IV: Office of Research Administration Review and Approval.

(a) *General.* Once Facility executives have approved a Research Project application, the application shall be sent to the Office of Research Administration via STAR. The Principal Investigator may not commence the Research Project until he/she has received final approval from the Office of Research Administration.

(b) *Office of Research Administration Review.* The application sent to the Office of Research Administration for review must be complete and accurate. The Office of Research Administration reserves the right to return a Facility-approved (i.e., approved by a FRRC and executive leadership) Research Project if the information it receives is insufficient to make a determination. In order to make its determination, the Office of Research Administration must receive from the FRRC, at a minimum:

(i) The completed application,

(ii) A copy of the IRB approved Human Subject Informed Consent form(s), assent form or approved waiver of consent, as applicable, to the extent they are not included in the completed application;

(iii) A copy of the IRB approved Research Authorization Form, any IRB waivers of the HIPAA authorization requirements described in H+H HIPAA Clinical Investigation and Research Policy and Guidelines, at Sections 3.0 through 3.3, to the extent they are not included in the completed application; and

(iv) Any such other documentation requested by the Office of Research Administration.

(c) *H+H Approval Communicated to Principal Investigator.* The Office of Research Administration, via STAR, will promptly notify the Principal Investigator, the FRC, the FRRC and executive leadership of final approval. Only at this point can the Research Project commence at the Facility.

If multiple Facilities are involved in a Research Project, H+H approval is granted per Facility.

4.2.5 *Duration of H+H Approval.* H+H approval will expire on the Research Project's IRB expiration date that was entered into STAR.

4.2.6 *Modifications.* If Principal Investigators update Research Project materials or tools, they should upload the IRB approved documents to STAR as they become available. Amendments do not require approval by the Facility or Office of Research Administration if the modification is not substantive.

4.2.7 *Reports of Referrals and/or Transfers.* Prior to referring and/or transferring a Human Subject enrolled in Research or a Research Project at an H+H Facility to non-H+H Facility, the Principal Investigator must submit the referral and/or transfer request to H+H Medical Director for review and approval. In the event of an emergency, the Principal Investigator may seek review and approval from the Executive Director or Medical Director of the Facility from which the Human Subject will be referred or transferred. In such an emergency situation, the Principal Investigator must notify the Medical Director of the referral or transfer as soon as possible but in no case more than seventy-two (72) hours after the referral or transfer.

SECTION 5. INFORMED CONSENT

5.1 **Policy.**

Informed Consent is a process that ensures that Human Subjects have been provided with sufficient information about the Research Project so that they may understand the nature of the Research and can knowledgeably and voluntarily decide whether or not to participate. A primary ethical responsibility of the Principal Investigator is to ensure that potential Human Subjects have been provided with all the information they might reasonably need to know. Any Research Project

utilizing Human Subjects requires the Informed Consent of those participants. Informed Consent is an ongoing exchange of information between the Research Team and the Human Subject that begins when a prospective Human Subject is initially informed about the Research, generally at the time of recruitment, and continues throughout the course of the Research Project. Informed Consent includes Human Subject recruitment materials, question/answer sessions, methods and materials used to obtain the Human Subject's consent to participate in the Research, and any other communication between the Human Subject and Research staff that explains or clarifies the Research to be conducted.

In order for the IRB to evaluate the consent process to ensure that it is adequate, the Principal Investigator must describe consent procedures and provide all consenting documents as a part of the application for IRB review of the Research Project. In situations where the ability of the Human Subject to understand the consent document is in question (e.g., if the document includes complex scientific information, or if the Human Subject may be educationally or cognitively impaired), additional considerations and procedures may be required. Please see Section 7 for additional protections afforded vulnerable populations and special classes of Human Subjects.

It is the policy of H+H that no one may involve a Human Subject as a participant in Research unless the Principal Investigator or an authorized designee has obtained either 1) the legally effective Informed Consent of the Human Subject or the Human Subject's legally authorized representative in an IRB-approved form, or 2) IRB approval for a waiver of Informed Consent in accordance with DHHS and FDA regulations.²³

5.2 Procedure.

5.2.1 Elements of Informed Consent

(a) *General Requirements for Informed Consent*²⁴

(i) Before involving a Human Subject in Research, a Principal Investigator or co-investigator shall obtain the validly executed Informed Consent of the Human Subject or the Human Subject's legally authorized representative.

(ii) A Principal Investigator or co-investigator shall seek Informed Consent only under circumstances that provide the prospective Human Subject or legally authorized representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence.

(iii) The information that is given to the Human Subject or the legally authorized representative shall be in language understandable to the Human Subject or legally authorized representative.

(iv) The prospective Human 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.

(v) Except for broad consent obtained in accordance with Subsection 5.2.1(d), below:

(1) Informed Consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective Human 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;

(2) Informed Consent as a whole must present information in sufficient detail relating to the Research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective Human Subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.

(b) *Basic Elements of Consent*

Informed Consent documents or other methods used to obtain consent must include the basic requirements of DHHS²⁵ and FDA regulations²⁶ (for Research Projects regulated by the FDA), unless a waiver or alteration of the document has been approved by the IRB. Additionally, there may be further requirements set forth under New York Public Health Law Article 24-A, as well as New York Civil Right Law § 79-l with regard to research involving genetic testing (see Section 21 of these Policies and Procedures, "Guidelines for the Use and Disclosure of Genetic Information"). The IRB has the authority to make the determination regarding the adequacy of the information in consent documents.

The requirements under DHHS are as follows:

(i) A statement that the Research Project involves Research, an explanation of the purposes of the Research, expected duration of the Human Subject's participation, description of the procedures to be followed, and identification of any procedures that are experimental;

(ii) A description of any reasonably foreseeable risks or discomforts to the Human Subject;

(iii) A description of any benefits to the Human Subject or to others that may reasonably be expected from the Research;

(iv) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the Human Subject;

(v) A statement describing the extent, if any, to which confidentiality of records identifying the Human Subject will be

maintained. (FDA Research Projects must also state the "...possibility that the Food and Drug Administration may inspect the records.");

(vi) For Research involving more than minimal risk,²⁷ an explanation as to whether any compensation or medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

(vii) Information regarding whom to contact for pertinent questions about the Research and Human Subjects' rights and whom to contact in the event of a research-related injury to the Human Subject;

(viii) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the Human Subject is otherwise entitled, and the Human Subject may discontinue participation at any time without penalty or loss of benefits to which the Human Subject is otherwise entitled;

(ix) One of the following statements about any Research that involves the collection of identifiable private information or identifiable biospecimens:

(1) 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 Principal Investigator or co-investigator for future Research studies without additional Informed Consent from the Human Subject or the legally authorized representative, if this might be a possibility; or

(2) A statement that the Human Subject's information or biospecimens collected as part of the Research, even if identifiers are removed, will not be used or distributed for future Research studies.

(c) *Additional Elements of Consent.* When reviewing a Research Project, the IRB will consider the need for inclusion of additional elements of consent.

(i) Except as provided in Subsection 5.2.2, or unless a waiver or alteration of the Informed Consent has been approved by the IRB, the Federal regulations indicate that one or more of the following elements of information, when appropriate, shall be provided to each Human Subject or legally authorized representative:

(1) A statement that the particular treatment or procedure may involve risks to the Human Subject (or to the embryo

or fetus, if the Human Subject is or may become pregnant) that are currently unforeseeable;

(2) Anticipated circumstances under which the Human Subject's participation may be terminated by the Principal Investigator without regard to the Human Subject's or legally authorized representative's consent;

(3) Any additional costs to the Human Subject that may result from participation in the Research;

(4) The consequences of a Human Subject's decision to withdraw from the Research and procedures for orderly termination of participation by the Human Subject, which may also ensure that a Human Subject's subsequent withdrawal from the study does not result in penalty or loss of benefits to which the Human Subject is otherwise entitled;

(5) A statement that significant new findings developed during the course of the Research that may relate to the Human Subject's willingness to continue participation will be provided to the Human Subject;

(6) The approximate number of Human Subjects expected to participate in the Research Project;

(7) A statement that the Human Subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the Human Subject will or will not share in this commercial profit;

(8) A statement regarding whether clinically relevant Research results, including individual Research results, will be disclosed to Human Subject, and if so, under what conditions; and

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

(ii) In addition to the requirements listed above, the IRB may further require the inclusion of any of the following:

(1) Identification of the Sponsor in Sponsor-initiated Research Projects;

(2) If blood samples will be drawn, information regarding the amount of blood that will be drawn;

(3) If Human Subjects are being followed for survival, indication of the Principal Investigator's intent to do so;

(4) If material such as tumor tissue, bone marrow, blood, etc. will be turned into a commercial product, a statement that the Human Subjects may not benefit from the development of the commercial product;

(5) The amount of compensation, and whether payment will be made incrementally or paid in full upon completion;

(6) When applicable, information that compensation of \$600 or more paid to Human Subjects within one calendar year is required to be reported to the IRS; or

(7) A disclosure statement if the Principal Investigator or a co-investigator is being directly compensated for conducting the Research Project or has a significant financial conflict of interest.

5.2.2 Broad Consent.

Broad consent may be obtained as an alternative to the Informed Consent obtained in accordance with Subsection 5.2.1 only with respect to the storage, maintenance, and secondary Research uses of identifiable private information and identifiable biospecimens. If the Human Subject or the legally authorized representative is asked to provide broad consent, the following shall be provided to each Human Subject or the Human Subject's legally authorized representative;

(a) The information required in Subsections 5.2.1(b)(ii); 5.2.1(b)(iii); 5.2.1(b)(v); 5.2.1(b)(viii); and when appropriate, 5.2.1(c)(i)(7) and 5.2.1(c)(i)(9);

(b) A general description of the types of Research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of Research conducted;

(c) A description of the identifiable private information or identifiable biospecimens that might be used in Research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researchers that might conduct Research with the identifiable private information or identifiable biospecimens;

(d) A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the

identifiable private information or identifiable biospecimens may be used for Research purposes (which period of time could be indefinite);

(e) Unless the Human Subject or legally authorized representative will be provided details about specific Research studies, a statement that they will not be informed of the details of any specific Research studies that might be conducted using the Human Subject's identifiable private information or identifiable biospecimens, including the purposes of the Research, and that they might have chosen not to consent to some of those specific Research studies;

(f) Unless it is known that clinically relevant Research results, including individual Research results, will be disclosed to the Human Subject in all circumstances, a statement that such results may not be disclosed to the Human Subject; and

(g) An explanation of whom to contact for answers to questions about the Human Subject's rights and about storage and use of the Human Subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of a Research related harm.²⁸

5.2.3 Posting of clinical trial consent form.

(a) For each clinical trial conducted or supported by a Federal department or agency, one IRB-approved Informed Consent form used to enroll Human Subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal website that will be established as a repository for such Informed Consent forms.

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

(c) The Informed Consent form must be posted on the Federal website after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any Human Subject, as required by the protocol.

5.2.4 Projects Involving FDA Investigational Drugs, Agents or Biologics. The requirements for Informed Consent for Research Projects involving an FDA investigational drug, agent, or biologic, are very similar to those listed above. Additional IRB consent requirements may include, when applicable, that:

(a) The document must contain a statement that the drug, agent or biologic is "investigational" or "not FDA-approved";

(b) No claims may be made which state or imply, directly or indirectly, that the drug, agent or biologic is safe or effective for the purpose(s) under investigation or that the product is in any way superior to another product;

(c) The document must describe any plans for randomization;

(d) The document must describe any plans for use of a placebo and the probability of the Human Subject receiving an active or inert substance;

(e) For phase I Research Projects, the consent document must disclose that the purpose of the Research includes examining the safety and toxicity of the drug, agent, or biologic. For phase II and phase III Research Projects, the consent document must disclose that the purpose of the Research includes examining the drug, agent, or biologic for safety and efficacy (effectiveness); and

(f) The document must include the conditions for breaking the code if the Research Project is blinded.

(g) *Projects Involving FDA Investigational Devices.* If the project involves an FDA investigational device, additional IRB consent requirements may include, when applicable, that:

(i) No claims may be made which state or imply, directly or indirectly, that the device is safe or effective for the purposes under investigation or that the device is in any way superior to any other device; and

(ii) The consent document must contain a statement that the device is “investigational,” or that it is “not FDA approved.”

5.2.5 Waiver or Alteration of Consent Requirements

A Principal Investigator seeking approval should be aware of the following:

(a) *Waiver or Alteration of Consent Requirements for Non-FDA Regulated Studies.* Under DHHS 45 C.F.R. § 46.116, the IRB may waive or alter the requirements for obtaining Informed Consent provided the IRB finds and documents that the requirements of Subsection 5.2.5(a)(iii), below, are satisfied. A data sharing agreement may be required; please consult the Office of Research Administration.

(i) *Waiver Generally.* The IRB may waive the requirement to obtain Informed Consent for Research under Subsections 5.2.1(a) through 5.2.1(c) provided the IRB satisfies the requirements of Subsection 5.2.5(a)(iii). If a Human Subject was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with Subsection 5.2.2, above, and refused to consent, the IRB cannot waive consent for the

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

(ii) *Alteration Generally.* An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of Informed Consent set forth in Subsections 5.2.1(b) and 5.2.1(c), provided the IRB satisfies the requirements of Subsection 5.2.5(a)(iii), below. The IRB may not omit or alter any of the requirements described in Subsection 5.2.1(a). The IRB may not omit or alter any of the elements of broad consent for the storage, maintenance, and secondary research use of identifiable information or identifiable biospecimens required under Subsection 5.2.2.

(iii) *Requirements for Waiver or Alteration.* In order for the IRB to waive or alter consent as described in this Subsection 5.2.5, the IRB must find and document the following:

(1) For studies with no more than minimal risk.

- a. The Research is not FDA-regulated;
- b. The Research involves no more than minimal risk to the Human Subjects;
- c. The Research could not practicably be carried out without the waiver or alteration;
- d. If the Research involves using identifiable private information or identifiable biospecimens, the Research could not practicably be carried out without using such information or biospecimens in an identifiable format;
- e. The waiver or alteration will not adversely affect the rights and welfare of the Human Subjects; and
- f. Whenever appropriate, the Human Subjects will be provided with additional pertinent information after participation.

(2) Additional Requirements for Government conducted or approved studies.

- a. The Research is not FDA-regulated;
- b. 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 research, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those

programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and

c. The Research could not practicably be carried out without the waiver or alteration.

(b) *FDA Regulated Studies.* For FDA-regulated research, the exceptions to Informed Consent requirements at 21 C.F.R. § 50.23 generally apply to emergency situations where all of the following circumstances are present:

(i) The Human Subject is confronted with a life-threatening situation;

(ii) Informed Consent is not possible because of an inability to communicate with, or obtain legally effective Informed Consent from, the Human Subject;

(iii) Time is not sufficient to obtain consent from the Human Subject's legally authorized representative; and

(iv) No alternative method of approved therapy is available that provides equal or greater likelihood of saving the Human Subject's life.

Also refer to Section 17.3.3 (Emergency Use of a Test Article) of these Policies and Procedures.

5.2.6 Documenting Consent

(a) *Generally.* In general, Informed Consent must be documented by the use of a written informed consent form approved by the IRB and signed (including in an electronic format) by the Human Subject or the Human Subject's legally authorized representative unless the IRB has determined that it can be waived under DHHS 45 C.F.R. § 46.117(c) or FDA 21 C.F.R. § 56.109(c). For Research Projects that involve FDA regulated products, investigators are responsible for adhering to any other FDA guidelines regarding documentation of consent that are applicable to the type of Research being conducted including the dating of the consent document by the Human Subject or the Human Subject's legally authorized representative. In all cases, the Human Subject or the Human Subject's representative should be given adequate opportunity to read the consent document and have questions answered before the document is signed.

(i) Except as outlined in Section 5.2.6(b) below, the Informed Consent form may be either of the following:

(1) A written Informed Consent form that meets the applicable requirements of Subsection 5.2.1, above. The Principal Investigator shall give either the Human Subject or the Human

Subject's legally authorized representative adequate opportunity to read the Informed Consent form before it is signed; alternatively, this form may be read to the Human Subject or the Human Subject's legally authorized representative;

(2) A short form written Informed Consent form stating that the elements of Informed Consent required by Subsection 5.2.1, above, have been presented orally to the Human Subject or the Human Subject's legally authorized representative, and that key information required by Subsection 5.2.1(a)(v)(1), above was presented first to the Human Subject before other information, if any, was provided. The IRB shall approve a written summary of what is to be said to the Human Subject or the legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Only the short form itself is to be signed by the Human Subject or the Human Subject's legally authorized representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the Human Subject or the Human Subject's legally authorized representative, in addition to a copy of the short form.

(ii) The Human Subject or the Human Subject's legally authorized representative will be given a copy of the consent document unless waived by the IRB per Subsection 5.2.6(b) below.

(b) *Waiver of Documentation of Informed Consent.*

(i) The IRB is also permitted by Federal regulations²⁹ to waive the documentation of Informed Consent (the use of a written consent form), provided that either:

(1) The only record linking the Human Subject and the Research Project would be the Informed Consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each Human Subject will be asked whether he or she wants documentation linking him or her with the Research Project, and the Human Subject's wishes will govern; or

(2) The Research Project presents no more than minimal risk of harm to Human Subjects and involves no procedures for which written consent is normally required outside the research context; or

(3) If Human Subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the Research presents no more than minimal risk of harm to Human

Subjects provided there is an appropriate alternative mechanism for documenting that Informed Consent was obtained.

(ii) In cases in which the documentation requirement is waived, the IRB may require the Principal Investigator to provide a Human Subject or legally authorized representative, with a written statement regarding the Research Project.

(c) *Requirements for Documentation of Consent When Some or All Elements of Consent are Waived.* If only some elements of Informed Consent are waived, documentation of partial consent may still be required, depending on the type of Research Project. If all elements of consent are waived, documentation of consent is also waived.

5.2.7 Exculpatory Language in Informed Consent Documents

Federal policy provides that no Informed Consent, whether oral or written may include any exculpatory language, through which the Human Subject or the legally authorized representative is made to waive or appear to waive any of the Human Subject's legal rights or releases or appears to release the Principal Investigator, the Sponsor, the institution or its agents from liability for negligence. OHRP and the FDA have applied a broad interpretation to the exculpatory language prohibition, as opposed to a narrow reading. In general, exculpatory statements relate to the releasing of liability or fault for wrongful acts.

An example of an acceptable clause in a consent form is:

H+H is not able to offer financial compensation nor to absorb the costs of medical treatment should you be injured as a result of participating in this research.

Examples of unacceptable language are:

I understand that I will not sue the sponsor or investigator for any negligence.

- or -

You agree to hold harmless the institution, investigators, and sponsors affiliated with or in any way a part of this research protocol.

5.2.8 Use of IRB-Approved Consent Documents. An IRB-approved consent, authorization, and assent (if applicable) must be used in the consenting process. The IRB stamps and indicates the approval period on the document. Consent documents that Human Subjects sign must bear a legible, dated IRB approval that is currently valid. If consent will be obtained orally (in person or by phone) or by email, the script/text to be used and method for documenting consent requires IRB approval prior to use.

5.2.9 Informed Consent Templates. The IRB may have developed templates for written consent, permission, and assent documents that provide investigators with guidance in development of the forms. Use of the templates helps ensure that all required elements are

incorporated into the document(s) and facilitates IRB review. Principal Investigators are encouraged to contact the applicable IRB for these forms.

5.2.10 Sponsor-Prepared Consent Documents. While Principal Investigators may utilize sample or draft consent documents developed by a Sponsor or Grantor, the IRB has final authority regarding approval of the consent document that is presented to prospective Human Subjects.

5.2.11 Revision of Consent Documents During the Research Project. Research Project protocols often change during the course of a Research Project which may require revisions to the consenting document(s). The revised document(s) may not be used until IRB approval has been obtained.

5.2.12 Providing Enrolled Human Subjects with Important New Information. Human Subjects enrolled in a Research Project should be kept informed of any new information relative to the Research Project that might affect their decision to continue participation. Whenever possible, this information should be presented to them in written form and Human Subjects should be asked to sign a copy of the notice/form indicating their receipt of the information. When the new information requires a change to the consent document, the enrolled Human Subject may need to be re-consented. Any new or revised documents that will be presented to Human Subjects require IRB review and approval prior to use.

5.2.13 Missing Signatures or Dates on Consent Documents. In all cases, signatures and dates on consent documents may only be provided by the individual(s) who signs the documents. If a signature or date is later found to be missing, procedures are as follows:

(a) If a Human Subject's signature is later found to be missing on a consent document, this information must be documented in the Human Subject's file and in the Research Project records, as appropriate. The information should not be filled in. The IRB must be notified immediately upon discovery of the omission that the consenting document is missing the Human Subject's signature. The IRB will instruct the Principal Investigator on how to proceed. Measures should be taken to prevent future omissions of Human Subject signatures on consenting documents.

(b) If a date is later found to be missing on a consent document, the information must be documented in the Human Subject's file and in the Research Project records, as appropriate. The information should not be filled in. The IRB must be notified promptly upon discovery of the omission that the consenting document is missing the signature date. The IRB will instruct the Principal Investigator on how to proceed. Measures should be taken to prevent future omissions of the signature date.

5.2.14 Documenting the Time of Consent. In some instances, it may be critical to document not only the date but also the time when consent was obtained. In such instances, the "time of signature" may be added to the signature area of the consent document.

SECTION 6. RESEARCH INVOLVING RECOMBINANT DNA

6.1 Definitions:

For purposes of this Section 6 , the following definitions shall apply:

“Human Gene Transfer” means the deliberate transfer into Human Subjects of either:

- (i) Recombinant nucleic acid molecules, or DNA or RNA derived from recombinant nucleic acid molecules, or
- (ii) Synthetic nucleic acid molecules, or DNA or RNA derived from synthetic nucleic acid molecules that meet any one of the following criteria:
 - a. Contain more than 100 nucleotides; or
 - b. Possess biological properties that enable integration into the genome (e.g., cis elements involved in integration); or
 - c. Have the potential to replicate in a cell; or
 - d. Can be translated or transcribed.³⁰

“Recombinant and Synthetic Nucleic Acid Molecules” means:

- (i) Molecules that a) are constructed by joining nucleic acid molecules and b) that can replicate in a living cell, i.e., recombinant nucleic acids;
- (ii) Nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, i.e., synthetic nucleic acids; or
- (iii) Molecules that result from the replication of those described in (i) or (ii) above.³¹

6.2 Policy:

H+H is responsible for ensuring that all Research involving Human Subjects and Recombinant or Synthetic Nucleic Acid Molecules and Human Gene Transfer conducted at H+H is conducted in compliance with the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules³² (the “NIH Guidelines”), the CDC guidelines on Biosafety in Microbiology and Biomedical Laboratories,³³ New York Pub. Health Law Part 32-A, and 10 NYCRR Part 61. The NIH Guidelines provide safety practices and containment procedures for Research involving Recombinant or Synthetic Nucleic Acid Molecules, including the creation and use of organisms and viruses containing Recombinant or Synthetic Nucleic Acid Molecules. H+H’s responsibilities include but are not limited to either establishing and maintaining internally or engaging and registering an externally administrated Institutional Biosafety Committee (“IBC”) that shall review all Research proposals or protocols and ongoing Research Projects involving the use of Recombinant or Synthetic Nucleic Acid Molecules or Human Gene Transfer for compliance with

the NIH Guidelines, as well as appointing a Biological Safety Officer where certain types of Research are being performed.³⁴ H+H is also responsible for ensuring Principal Investigators and laboratory staff have adequate expertise and training.³⁵ In addition, H+H is responsible for obtaining NYSDOH approval for any Research Project involving recombinant DNA.³⁶

6.3 Procedure:

6.3.1 *General*

(a) The Principal Investigator shall ensure that no Human Subject shall be enrolled in a Human Gene Transfer experiment until the NIH protocol registration process has been completed, as further discussed in Section 6.3.2(b) below, IBC and IRB approval has been obtained, and all applicable regulatory authorization(s) have been obtained.³⁷

6.3.2 *Research Proposals and Protocols*

(a) In addition to the Research Approval Process set forth in Section 4 of these Policies and Procedures, the Principal Investigator must submit a proposed Research Project involving Human Subjects and Recombinant or Synthetic Nucleic Acid Molecules or Human Gene Transfer that is to be conducted at H+H to the applicable IBC for review and approval in accordance with the IBC's submission requirements.³⁸

(b) Principal Investigators involved in Human Gene Transfer Research are required to obtain additional approvals from the NIH³⁹ and must review Appendix M of the NIH Guidelines, "Points to Consider in the Design and Submission of Protocols for the Transfer of Recombinant DNA Molecules into One or More Human Subjects,"⁴⁰ which includes adverse event/safety reporting requirements for those Principal Investigators who have received approval from the FDA to initiate a Human Gene Transfer protocol. Principal Investigators involved in such protocols must follow all applicable requirements set out in Appendix M of the NIH Guidelines including, but not limited to, those for protocol submissions,⁴¹ and all reporting requirements,⁴² including reporting any serious adverse event immediately to the IBC, OHRP, Office of Biotechnology Activities of NIH, and FDA, followed by the submission of a written report filed with each group.

(c) Approval by the IBC, in and of itself shall not constitute approval for full implementation since a Research Project is subject to review and disapproval through H+H's Research Approval Process. In turn, H+H may not approve the conduct of a Research Project involving Recombinant or Synthetic Nucleic Acid Molecules that has been disapproved by the relevant IBC.

6.3.3 *Principal Investigator Responsibilities After Recombinant DNA Research Approval.* Once the Principal Investigator has received both IBC and H+H approval to conduct Human Subject Research involving Recombinant or Synthetic Nucleic Acid Molecules, the Principal Investigator shall have the following responsibilities:⁴³

- (a) Make available to all laboratory staff the protocols that describe the potential biohazards and the precautions to be taken;
- (b) Instruct and train laboratory staff in the practices and techniques required to ensure safety, and the procedures for dealing with accidents; and
- (c) Inform the laboratory staff of the reasons and provisions for any precautionary medical practices advised or requested (e.g., vaccinations or serum collection);
- (d) Supervise the safety performance of the laboratory staff to ensure that the required safety practices and techniques are employed;
- (e) Investigate and report any significant problems pertaining to the operation and implementation of containment practices and procedures in writing to the Biological Safety Officer (where applicable), IBC, NIH Office of Science Policy (“OSP”), and other appropriate authorities (if applicable). Reports to NIH OSP shall be sent to the Office of Science Policy, National Institutes of Health by e-mail to: NIHGuidelines@od.nih.gov, the Office of Research Administration, FRRC, and other appropriate H+H and governmental authorities (if applicable);
- (f) Correct work errors and conditions that may result in the release of Recombinant or Synthetic Nucleic Acid Molecule materials;
- (g) Ensure the integrity of the physical containment (e.g., biological safety cabinets) and the biological containment (e.g., purity and genotypic and phenotypic characteristics); and
- (h) Comply with reporting requirements for Human Gene Transfer experiments conducted in compliance with the NIH Guidelines.

SECTION 7. RESEARCH CONDUCTED ON VULNERABLE POPULATIONS AND OTHER SPECIAL CLASSES

7.1 Policy

H+H recognizes the need to protect individuals or categories of individuals who are subject to coercion or undue influence. Consequently, when assembling the application to be submitted to the IRB and approval submissions discussed in Section 4 and Section 12 (Research Approval Process and Continuing Approval, respectively), the Principal Investigator should be mindful of Human Subjects who are likely to be vulnerable to coercion or undue influence and the regulatory requirements that must be met before an IRB can approve a protocol or proposed consent form involving such Human Subjects. These classes include children, prisoners, fetuses and neonates, and individuals with impaired decision-making capacity. In addition to the above, there are several populations that should also be given special consideration and may require additional safeguards. These groups include, but are not limited to pregnant women, students in schools, economically or educationally disadvantaged persons, undocumented individuals and non-English speakers.

7.2 Procedures.

7.2.1 *Children.*

(a) Research Projects involving 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, are considered Research involving children and are subject to the requirements of Federal and New York State law. Under New York law, persons less than 18 years of age are considered children.⁴⁴

(b) In its consideration of a Research Project involving children as Human Subjects, the IRB generally contemplates the level of risk to the children and whether the Research Project presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.⁴⁵ Regardless of the level of risk involved, the Principal Investigator must provide for the adequate solicitation of assent of the children, where appropriate, and the permission of their parents or legal guardians in accordance with the requirements of 45 C.F.R. §§ 46.116, and 46.405 through 46.408.⁴⁶ In some circumstances, New York law allows for children to provide their own consent, such as in the case of emancipated minors, and minors who understand the benefits and risks for proposed alternative treatments with respect to their reproductive health and sexually transmitted diseases, some mental health services, alcohol and drug treatment services, and sexual assault treatment.

(c) The FRRC or the Office of Research Administration in their respective reviews during the Research Approval Process (Section 4) and Continuing Approval (Section 12) may inquire of the IRB the basis upon which it approved the participation of children in a Research Protocol.

7.2.2 *Children who Reach the Age of 18 During the Course of Participation.*

(a) Where a Research Project includes Human Subjects who were enrolled in the Research Project as children but will reach the age of 18 during the course of participation, that Human Subject's participation is no longer regulated by the requirements of 45 C.F.R. § 46.408 regarding parental or guardian permission and subject assent.⁴⁷

(b) The Principal Investigator should consult with the applicable IRB, with guidance from the Sponsor or Grantor, to determine whether the requirements for obtaining Informed Consent can be waived or the Principal Investigator should seek new Informed Consent for the now adult-subject for any ongoing interactions or interventions or the use of biological specimens collected while the Human Subject was a child.

(c) If the Research Project procedures and interventions have been completed and the Human Subject is in long-term follow-up involving data collection only, the Principal Investigator should consult with the applicable IRB

to determine whether an addendum to the consent for continued data collection may be used.

7.2.3 *Children Who are Wards of the State.*

(a) Federal and New York State law regulate the conduct of research that involves children who are considered to be wards of the state. Under Federal and State law, the term “ward” is generally meant to refer to children who are in the custody of the state or a social service agency.⁴⁸ Under New York State law, children in foster care are considered wards of the state.⁴⁹ Questions that arise as to whether a child should be considered a ward of the state under these Policies and Procedures should be directed to the Office of Legal Affairs.

(b) Research Projects involving children who are wards of the state may occur only if the IRB determines the Research Project is either related to the Human Subject’s status as a ward, or is conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.⁵⁰

(c) If the IRB approves a Research Project involving wards, the Principal Investigator will be required to appoint an advocate, in addition to any other individual acting on behalf of the child as guardian or in loco parentis, for each child who is a ward. One individual may serve as advocate for more than one child. An individual who is appointed as an advocate for a ward must:

(i) Have the background and experience to act in and agree to act in the best interest of the child for the duration of the child’s participation in the Research Project; and

(ii) Not be associated in any way (except in the role as advocate or member of the IRB) with the Research Project, the Principal Investigator(s) or the guardian organization.⁵¹

(d) In addition, the Principal Investigator must provide for the adequate solicitation of assent of the children, where appropriate, and the permission of their parents or legal guardians in accordance with the requirements of 45 C.F.R. §§ 46.116 and 46.408.⁵²

(e) Research involving the New York Office of Children and Family Services (“OCFS”)⁵³

(i) Research Projects involving children in programs operated, regulated, or supervised by OCFS, including residential and community-based services administered by OCFS as well as Child Protective Services (“CPS”), Preventive Services, Foster Care, and Adoption, must obtain approval from OCFS before initiating such Research.⁵⁴ Prior to submitting a research proposal to OCFS for review, the Principal Investigator must obtain all of the following approvals:

(1) Prior approval from the IRB (a copy of the signed IRB approval document must be provided to OCFS at the time the research proposal is submitted for review);

(2) If the Research Project involves child welfare cases, a letter from each local social services department and each voluntary agency responsible for the cases involved in the Research Project;

(3) If the Research Project involves New York City Administration for Children's Services (ACS) cases, a final letter of approval from ACS, as described in greater detail in 7.2.3(f) below;

(4) If the Research Project involves children in OCFS custody, a letter of approval from the OCFS Deputy Commissioner for the Division of Juvenile Justice and Opportunities for Youth.

(ii) A Principal Investigator who engages in a Research Project regulated by OCFS must understand and adhere to all applicable OCFS requirements involving the conduct of such Research including, but not limited to, all applicable Informed Consent requirements. All requirements for Research regulated by OCFS, including all submission requirements for OCFS research review, are outlined in **Exhibit 6**.⁵⁵

(f) Research Involving the New York City Administration for Children's Services ("ACS").⁵⁶

(i) Research Projects involving children served by New York City ACS must obtain the approval of the ACS Research Review Committee before initiating such Research. Research Projects involving only case records or other data may be eligible for an expedited review. A Principal Investigator who engages in a Research Project regulated by ACS must understand and adhere to all applicable ACS requirements involving the conduct of such Research, including, but not limited to, all applicable Informed Consent requirements. All requirements for Research regulated by ACS, including all submission requirements for ACS research review, are outlined in **Exhibit 7**.

(ii) Use of Experimental Drugs. In general, ACS prohibits the use of experimental drugs in research involving wards of the state. Principal Investigators who wish to conduct Research involving experimental drugs and wards of the state in ACS custody should contact the Office of Research Administration and the Office of Legal Affairs for additional information.⁵⁷

(g) The FRRC or the Office of Research Administration in their respective reviews during the Research Approval Process (Section 4) and Continuing Approval (Section 12) may inquire of the IRB the basis upon which it approved the participation of wards in a Research Protocol.

7.2.4 *Pregnant Women⁵⁸, Fetuses and Neonates.*

(a) H+H considers the special needs of any pregnant women, fetuses and neonates enrolled in any Research Project and will comply with all applicable law for the protection of such Human Subjects. Pregnant women, fetuses and neonates, as those terms are defined in 45 C.F.R. § 46.202, may be involved in a Research Project and the IRB may approve such involvement if all conditions required under Federal regulations are met.⁵⁹ Generally, the IRB will weigh the potential risk to the pregnant woman, fetus or neonate against the benefit for the pregnant woman, fetus or neonate and the possibility of obtaining important biomedical knowledge from the Research Project. In addition, with respect to neonates, the IRB considers whether a determination of the viability of the neonate has been made, and by whom.

(b) The Principal Investigator should consult with the IRB with respect to the contents of the Informed Consent. Some considerations the Principal Investigator should be mindful of are as follows:

(i) In addition to the general Informed Consent requirements under 45 C.F.R. Part 46, certain disclosures regarding the foreseeable impact of the Research on the fetus or neonate must be made.

(ii) In certain situations, such as Research benefiting only the fetus (and not the pregnant woman), the father's consent may also be required.

(iii) For children who are pregnant, assent and permission must be obtained in accordance with the provisions of 45 C.F.R. Part 46 relating to children.

7.2.5 *Prisoners.*

(a) Under the Federal regulations, prisoners (e.g. any individual involuntarily confined or detained in a penal institution, in other facilities by virtue of statutes, or commitment procedures which provide alternatives to criminal prosecution, and those detained pending arraignment, trial or sentencing), may participate in a Research Project as a Human Subject only if approved by the IRB. In order to obtain approval of such Research Projects, the Principal Investigator must demonstrate, generally, the following:⁶⁰

(i) The Research Project relates to the study of incarceration, criminal behavior, prison conditions or other issues related to the Human Subject's status as a prisoner, or that the Research Project have the intent and reasonable probability of improving the health or well-being of the Human Subject.

(ii) Any possible advantages accruing to the prisoner through participation in the Research Project, when compared to other general

conditions in the prison, are not of such a magnitude to impair the prisoner's ability to weigh the risks of Research Project participation against the benefits.

(iii) The risks involved are commensurate with risk that would be accepted by non-prisoner volunteers.

(iv) Procedures for the selection of Human Subjects are fair and immune from arbitrary intervention by prison authorities and prisoners, and that control Human Subjects must be selected randomly from similar prisoners.

(v) There are assurances that a parole board will not take into account the prisoner's participation.

(vi) Adequate provision for follow-up is made where needed, taking into account the varying lengths of the individual prisoner's sentence and each prisoner is informed of that provision prior to the prisoner's participation in the Research Protocol.

(vii) Information concerning a Research Protocol will be presented in language that the prisoner can understand.

(b) If the Research Protocol requires the assignments of prisoners to control groups which may not benefit from the Research Project, special approval must be obtained from DHHS.⁶¹

(c) With respect to Research involving prisoners, H+H, through the relevant Principal Investigator, shall make all necessary certifications to DHHS and/or NYSDOH, as applicable, regarding the use of prisoners in Research including (but not limited to) for Research supported by DHHS, that the reviewing IRB has made all necessary findings as required under 45 C.F.R. § 46.305(a).

7.2.6 Individuals with impaired decision-making ability and Individuals in OMH or OMRDD facilities.

(a) Use of Surrogate Permission. H+H holds the ethical position that the use of surrogate permission with individuals with impaired decision-making ability should generally follow the recommendations of the New York State Task Force on Life and the Law on Research with Human Subjects who lack consent capacity.⁶² This policy does not apply to the conduct of emergency Research under the FDA regulations 21 C.F.R. § 50.24.

(b) Enrollment of Individuals with Impaired Decision-Making Ability in Research. The IRB may allow the enrollment of individuals with impaired decision-making ability, with the permission of a legally authorized representative as described in this section, into a Research Project depending on the level of risk, the likelihood of benefit to the Human Subject and the possibility of yielding

knowledge about the Human Subject's disease/condition or improving the health or welfare of individuals with impaired decision-making ability. The IRB reviewing a protocol that involves individuals with impaired decision-making ability must follow relevant guidance of the OHRP, NIH and the New York State Task Force for Life and the Law with respect to its review and approval of such protocols.⁶³

(c) Contents of Research Protocol. In studies involving a subject population whose capacity is known to be impaired, or is highly likely to be impaired, the Principal Investigator must include in the Research Protocol the following:

(i) Adequate procedures for making and documenting the determination that a prospective Human Subject is an individual with impaired decision-making ability, including:

(1) Providing an explanation of why a particular screening tool will be used and how it accounts for the degree of impaired consent capacity for the Research population.

(2) Describing the qualifications of the person conducting the assessment and state whether the person is affiliated with the Research Project.

(3) Procedures for informing persons who are determined to have decisional incapacity of that determination prior to enrollment in a Research Project, and procedures to document that this has occurred.

(4) Procedures for informing Human Subjects that they may be enrolled in the Research only with permission of a legally authorized representative.

(5) Procedures to maintain participants' care, including personalized attention to ensure safety and the maintenance of required medical and therapeutic procedures, where appropriate.

(6) Appropriate procedures for the continuing/periodic capacity assessment of Human Subjects with impaired decision-making ability and their continued willingness to participate and re-consenting the Human Subject, as appropriate.

(7) Indication as to whether the results of the capacity assessment will be entered into the individual's medical record.

(8) Procedures for a withdrawal mechanism for the Research population:

a. With the least risk to the participant when reasonable and safe to do so,

b. Reporting to the IRB of record regarding the withdrawal, including the reason for the withdrawal and whether the withdrawal was from all aspects of the Research or only the primary interventional or procedural component, and who made the request for the withdrawal.

(9) For Protocols which involve high risk or no direct benefits to the participant, evidence of safety and efficacy data from studies conducted in a non-impaired group prior to inclusion of cognitively impaired individuals.

(d) Informed Consent and Legally Authorized Representatives.

(i) The Principal Investigator must obtain Informed Consent from a Human Subject's legally authorized representative in the same manner and extent as for adults with capacity (i.e., sufficient information provided to the representative, adequate understanding of the information by the representative, and voluntary agreement to enrollment on behalf of the subject).

(ii) H+H recognizes the health care surrogate pursuant to the New York State Family Health Care Decisions Act⁶⁴ as a legally authorized representative (listed in descending order of priority):

(1) A health care agent properly designated on a health care proxy form;

(2) A court-appointed guardian or committee under the New York Surrogates Court;

(3) Procedure Act Article 17-A;

(4) The spouse, unless legally separated from the participant, or the domestic partner;

(5) An adult son or daughter;

(6) A parent;

(7) An adult brother or sister; or

(8) A close friend, who is an adult (18 years or older) who has a close personal relationship with the Human Subject and provides a signed written statement (in a format approved by the IRB) to the Principal Investigator that they are a close friend of the Human Subject and that they have maintained such regular contact

with the Human Subject as to be familiar with the Human Subject's activities, health, religious or moral beliefs, and some means of corroborating such familiarity.

(iii) When a person with priority on this list is not reasonably available, not willing to make a decision, or not competent to make a decision regarding Research participation, the authority falls to the person of the next highest priority. Once identified, the identity of the surrogate will be documented in the Research records.

(iv) For Research that offers no prospect of direct benefit to the individual with impaired decision-making ability and involves either a minor increase over minimal risk, or more than a minor increase over minimal risk, H+H does not recognize as a legally authorized representative for purposes of this section any surrogate appointed through an institutional or judicial mechanism who has no prior relationship to the potential participant. Such surrogate may not enroll an individual with impaired decision-making ability into such Research Project.

(v) For Research that offers the prospect of direct benefit to the individual with impaired decision-making ability, H+H will recognize institutional or judicial appointed representatives where the IRB finds such representative's consent to be acceptable given the risk level of the Research Project and the prospect of direct benefit to the individual with impaired decision-making ability.

(vi) If more than one individual could be a surrogate under the New York State Family Health Care Decisions Acts and those individuals do not agree to the enrollment of the individual with impaired decision-making ability into a Research Project, such individual with impaired decision-making ability shall not be enrolled in such Research Project.

(vii) If the individual with impaired decision-making ability evidences any objection, verbal or otherwise, to being enrolled in the Research Project, such individual shall not be enrolled in such Research Project.

(e) Principal Investigator Responsibilities in Obtaining Informed Consent from Legally Authorized Representatives. When obtaining an Informed Consent from a legally authorized representative the consent procedures, information required in an Informed Consent, and any waiver or alteration requests related to the informed consent process and contents outlined in Section 5, "Informed Consent," above must be followed. In addition, the Principal Investigator must do the following:

(i) Provide a notice to the potential participant and legally authorized representative that an assessment will be conducted on the

potential participant and the consequences (if any) of a determination of incapacity.

(ii) Make efforts to ensure that potential participants and the legally authorized representative understand the difference between the goals of Research and the goals of clinical care to help dispel any therapeutic misconception around the Research.

(iii) Present information using methods that are appropriate to the consent capacity of the potential participant and attempt to provide information in a variety of ways.

(iv) Provide regular updates to the legally authorized representative and participant on the status of the participant and the progress of the Research Project.

(v) Principal Investigator should analyze whether the legally authorized representative might be the true beneficiary of any financial compensation offered or the enrollment might alleviate the burden of caring for the potential participant, to prevent undue inducement to consent to Research.

(vi) Principal Investigator must give the legally authorized representative a copy of the “*Guidance for Legally Authorized Representatives Enrolling Individuals with Impaired Decision Making Ability in Research Studies*”, attached here to as **Exhibit 8** and explain the guidance to the legally authorized representative.

(vii) Once the legally authorized representative has signed the acknowledgement on the “*Guidance for Legally Authorized Representatives Enrolling Individuals with Impaired Decision Making Ability in Research Studies*”, to the extent a written Informed Consent is required, the signed guidance should be appended to and maintained with the Informed Consent if in hard copy. If electronic, a scanned pdf should be kept.

(viii) If consent is obtained in person, the legally authorized representative’s consent signature will be obtained as follows:

(1) The legally authorized representative shall sign and date the Informed Consent document;

(2) When possible, the Human Subject shall sign and date assent;

(3) The person obtaining consent may also sign and date the document;

(4) A witness to the Human Subject's signature shall also sign and date the document if required by the study protocol, the IRB, or Sponsor.

(f) Consent of the Commissioner of Health. For non-federally regulated Research that involves adults with impaired decision-making abilities who are incompetent persons or mentally disabled persons, the consent of the Commissioner of Health is required, in addition to the consent of the legally authorized representative.⁶⁵

(g) Release of Clinical Records. For H+H Facilities licensed or operated by the New York State Office of Mental Health ("OMH") or Office for People with Developmental Disabilities ("OMRDD"), such Facilities may, with the consent of the relevant Office's commissioner, release patients' clinical records to qualified researchers upon approval of the IRB, the Office of Research Administration and any other applicable committee specially constituted for the approval of Research Projects at the Facility and H+H, provided that the researcher shall in no event disclose information tending to identify a patient or client.⁶⁶

*7.2.7 Alcohol and Substance Use Patients.*⁶⁷

(a) Coordination with Treatment Plan. The understanding, prevention, and amelioration of chemical abuse and dependence are enhanced by knowledge gained through Research. A patient receiving treatment for alcohol or substance use may participate in Research only if such Research does not conflict with his or her individual treatment plan. Participation as a "subject at risk" in any Research Project or activity shall not deprive any patient of the rights, privileges, and protections provided to all patients by this Part. "*Subject at risk*" means any individual who may be exposed to the possibility of injury, including physical, psychological or social injury, as a consequence of participation as a Human Subject in any Research, development or related activity which departs from the application of those established and accepted methods necessary to meet his or her needs or which increases the risks of daily life. The Research Project or activity must be approved by an independent IRB and the approval kept on file.

(b) *Approval of Research.* Approval of any Research on subjects at risk must be obtained in accordance with 45 C.F.R. Part 46.

(c) *Informed Consent.* Informed Consent of a patient who participates as a subject at risk in any Research Project shall be obtained in accordance with 45 C.F.R Part 46.

(d) *Reports to OASAS.* Research Projects which involve placing patients of a chemical dependence service at risk must be reported to the New York State Office of Alcoholism and Substance Abuse Services ("OASAS") prior to initiation of the project.

(e) *Release and Use of Clinical Records for Research Purposes.* For H+H Facilities licensed or operated by OASAS, such Facilities may, with the consent of the commissioner of OASAS, release patients' clinical records to qualified researchers upon approval of the IRB, the Office of Research Administration and any other applicable committee specially constituted for the approval of Research Projects at the Facility and H+H, provided that the such disclosure complies with the requirements of 42 C.F.R. § 2.52(a).⁶⁸

(i) Principal Investigators conducting research involving records released under Section 7.2.7(e), above, are fully bound by 42 C.F.R. Part 2 and, if necessary, will resist in judicial proceedings any efforts to obtain access to patient records except as permitted by law.⁶⁹

(ii) Any Principal Investigator using patient identifying information obtained under Section 7.2.7(e), above, who requests linkages to data sets from a data repository(-ies) holding patient identifying information must first obtain IRB approval of the request, and may not provide any patient identifying information to law enforcement agencies or officials.⁷⁰

7.2.8 *Research in Schools.*

(a) When a Research Project will be conducted in schools, the Principal Investigator must, in addition to 45 C.F.R. Part 46 subparts A and D, demonstrate that the Research Project accounts for protections required by the Family Educational Rights and Privacy Act (FERPA)⁷¹ and Protection of Pupil Rights Amendment (PPRA)⁷² are adequately met as described below. FERPA defines the rights of students and parents concerning the review, amendment, and disclosure of educational records. Research Projects involving surveys in schools are regulated under PPRA.

(b) The Principal Investigator, in developing the Research Protocol and seeking IRB approval, must provide for:

(i) Obtaining written parental permission prior to disclosure of personally identifiable information from a student's educational record;⁷³

(ii) Obtaining parental permission prior to inspecting student records if identifiers are linked to the data;

(iii) The opportunity for parents or guardians to inspect surveys, questionnaires, and instructional materials used in the Research Project;⁷⁴

(iv) Obtaining parental permission prior to a child's participation in a survey revealing information regarding: political affiliations or beliefs; mental or psychological problems; sexual behavior or attitudes; illegal, anti-social, self-incriminating, or demeaning behavior; critical appraisals of other individuals with whom respondents have close family relationships;

legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers; religious practices, affiliations, or beliefs; or income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such program);⁷⁵

(v) Compliance with the requirements of the New York City Department of Education Research Proposal Guidelines.⁷⁶

7.2.9 *Students, Employees and Others in Subordinate Positions.*

(a) Students, employees and other persons in subordinate positions or positions of lesser power or status provide a pool of easily accessible Human Subjects. There are no Federal regulations that specifically address the inclusion of these individuals in Research Projects. However, these participants are vulnerable to being unduly influenced by the expectation that participation or non-participation in a protocol may place them in good favor with faculty or senior staff (e.g., that participating will result in receiving better grades, recommendations, a promotion, or the like), or that failure to participate will negatively affect their relationship with faculty or senior staff generally (i.e., by seeming “uncooperative”).

(b) As such, the Principal Investigator must demonstrate that he or she will consider whether the autonomy and confidentiality of these individuals are adequately protected, including:

(i) That incentives for participation do not present undue influence;

(ii) That Human Subjects have the ability to decline participation;

(iii) That confidentiality is maintained for self-disclosures of a personal nature; and

(iv) For students, if course credit is given for participation, that alternatives that are no more burdensome than the participation in the Research Project are available for receiving equal credit.

7.2.10 *Other Groups Requiring Special Considerations.*

(a) The economically or educationally disadvantaged,⁷⁷ homeless persons, the elderly, members of particular minority groups, undocumented individuals and non-English speakers are only some of the additional populations that may require special protections in the Research environment. When such groups are specifically targeted as Human Subjects, the Principal Investigator must demonstrate that adequate safeguards are in place to protect such subject groups

from risks unique to the population and that researcher does not use his or her position to unduly influence participation.

SECTION 8. CERTIFICATES OF CONFIDENTIALITY

8.1 Policy.

A Certificate of Confidentiality (“CoC”) protects the privacy of Human Subjects enrolled in biomedical, behavioral, clinical and other forms of Research in which Identifiable Sensitive Information (as defined below) is collected, including Research on mental health and Research on the use and effect of alcohol and other psychoactive drugs.⁷⁸ CoCs are issued by DHHS’s NIH and other HHS agencies and are subject to the NIH Policy for Issuing Certificates of Confidentiality (“NIH Policy for CoCs”).⁷⁹

CoCs protect the privacy of Human Subjects by prohibiting researchers from disclosing to any other person not connected with the Research the names and any information, document, or biospecimen containing identifiable, sensitive information about a Human Subject, except in certain limited circumstances.⁸⁰ A CoC does not prevent disclosures that are made with the consent of a Human Subject, nor disclosures that are made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of Human Subjects in Research.⁸¹

Research funded by a non-HHS Federal Agency that uses sensitive identifiable information may request a CoC from the NIH.

If the Research is not Federally funded, a CoC may be issued upon application.⁸² For non-Federally funded Research, Principal Investigators should seek a CoC whenever Identifiable Sensitive Information, as defined below, will be collected or generated during the course of a Research Project. The Research Council shall develop guidelines for Principal Investigators to assist them in determining when to apply for a CoC.

8.2 Definitions.

The term “Identifiable Sensitive Information” means information that is about an individual and that is gathered or used during the course of biomedical, behavioral, clinical, or other research where the following may occur:

- An individual is identified; or
- For which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.⁸³

8.3 Procedure.

8.3.1 Generally

(a) It is the Principal Investigator's responsibility to consult with the applicable IRB with respect to its requirements for obtaining CoCs and informing Human Subjects of the protections of a CoC in the Informed Consent.

(b) A Principal Investigator who is conducting a Research Project that is subject to a CoC may not:

(i) Disclose or provide, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, the name of a Human Subject or any information, document, or biospecimen that contains Identifiable Sensitive Information about the Human Subject and that was created or compiled for the purposes of the Research Project, unless such disclosure or use is made with the consent of the Human Subject; or

(ii) Disclose or provide to any other person not connected with the Research Project the name of the Human Subject or any information, document, or biospecimen that contains Identifiable Sensitive Information about the Human Subject and that was created or compiled for purposes of the Research Project.⁸⁴

8.3.2 Federally Funded Research Projects.

(a) *NIH-Funded Research Projects*

(i) As of October 1, 2017, all NIH-funded Research Projects that were commenced or ongoing on or after December 13, 2016 and are within the scope of the NIH Policy on CoCs are deemed to have been automatically issued a CoC. The NIH will not provide documentation of individual CoCs.⁸⁵ Principal Investigators are responsible for determining whether a given Research Project falls within the scope of the NIH Policy for CoCs. For all NIH-funded Research Projects, Principal Investigators are required to submit written documentation to the Office of Research Administration detailing the applicability of the NIH Policy for CoCs, using the questions set forth in Section 8.3.2(a)(ii), below. The Principal Investigator must also include a copy of the applicable protocol and any other relevant documentation requested by the Office of Research Administration. The Office of Research Administration will review the Principal Investigator's written submission and determine whether or not the NIH Policy for CoCs applies to the Research Project in question.

(ii) The Principal Investigator must submit written documentation to the Office of Research Administration answering the following questions:

(1) Is the activity biomedical, behavioral, clinical, or other research?

(2) Does the Research involve Human Subjects?

(3) Does the Research involve the collection or use of biospecimens that are identifiable to an individual?

(4) If collecting or using biospecimens are part of the Research, is there a small risk that some combination of the biospecimen, a request for the biospecimens, and other available data sources could be used to deduce the identity of an individual?

(5) Does the Research involve the generation of individual level, human genomic data?

The Office of Research Administration will determine the applicability of the NIH Policy for CoCs based on the Principal Investigator's responses to the questions above, and on the other documentation submitted by the Principal Investigator to the Office of Research Administration.

(b) Other HHS-Funded Research (Non-NIH)

(i) Several non-NIH HHS agencies, including the Centers for Disease Control and Prevention ("CDC"), Food and Drug Administration ("FDA"), Health Resources & Services Administration ("HRSA"), and Substance Abuse and Mental Health Services Administration ("SAMHSA") issue CoCs. If a Research Project is funded by one of these agencies or is operating under the authority of the FDA, the Principal Investigator should contact the Certificate Coordinators at the funding agency to coordinate the issuance of a CoC.⁸⁶

(ii) If a Research Project is funded by an HHS agency other than NIH, CDC, FDA, HRSA, or SAMHSA that does not issue CoCs, the Principal Investigator may request a CoC using the NIH online application system, available at <https://humansubjects.nih.gov/coc/faqs>.

8.3.3 Non-Federally Funded Research. Principal Investigators conducting non-Federally funded Research Projects that would otherwise be covered under a CoC if Federally funded may apply for a CoC through the NIH online application system available at <https://humansubjects.nih.gov/coc/apply>.⁸⁷ Where the Principal Investigator applies for a CoC, both the Principal Investigator and Institutional Official must sign the CoC application.

8.3.4 Changes in Research Protocol. The Principal Investigator is responsible for notifying the NIH (and/or other applicable issuing agency) of any changes to the Research Protocol, such as major changes in the scope or direction of the Research Protocol, changes in personnel having major responsibilities in the Research Project, or changes in the drugs, if any, to be administered or persons administering.

8.3.5 Extension of CoCs. Where a Research Project extends beyond the expiration date of the CoC, the Principal Investigator should submit a written request for an extension of the date. The request should be submitted at least three (3) months prior to the CoC's expiration. Such request must include an explanation of the reasons for requesting an extension, a

revised estimate of the date for completion of the Research Project, documentation of the IRB's most recent approval for the Research Project, and a copy of the Informed Consent form, which should include language explaining the CoC's protections.

8.3.6 Limitations on Use of CoC. Once a CoC has been obtained, the Principal Investigator must refrain from representing the CoC as an endorsement of the Research Project by the Federal government, or otherwise using the CoC in a coercive manner when recruiting Human Subjects.

8.3.7 Demands for Disclosure. Upon receipt of any demand for disclosure of sensitive information of Human Subject, whether or not protected by CoC, the Principal Investigator should contact the Office of Legal Affairs immediately for further instructions.

SECTION 9. CONFLICTS OF INTEREST IN RESEARCH

9.1 Policy

Federal regulations of the DHHS require that institutional recipients of funding for Research collect and report information about individuals involved in Research regarding their relevant financial interests related to their roles in the institution or Research. This Section establishes policies and procedures regarding the obligations of these individuals in disclosing financial interests they or their family members may have in connection with their H+H responsibilities, and the obligations of H+H in reviewing, monitoring and reporting these interests.

H+H recognizes that many investigators who are leaders in their field may serve in a number of capacities where there may, or may not be, potential conflict. This policy does not prohibit an individual to serve in an advisory capacity, receive Research funds or other activities that need to be disclosed; its intent is to facilitate the proper reporting and, if necessary, management of those interests.

For clinical studies subject to FDA regulations, Principal Investigators and Research Team members may have additional conflict of interest reporting obligations to the FDA and trial sponsor. To the extent funding is from sources other than a Federal agency, individuals involved in such Research should consult with the applicable IRB as to whether the below compliance with the Policy meets the requirements of such other funding sources.

In addition to this Section 9, Principal Investigators and Research Team members who are directly employed by H+H must also adhere to the conflict of interest provisions of Chapter 68 of the New York City Charter, and Research Team members who are Affiliate personnel must adhere to the conflict of interest provisions in H+H's Code of Ethics. Further, all Research Team members, whether employed directly or through an affiliation agreement or otherwise, must adhere to the H+H's Principles of Professional Conduct.

9.2 Definitions

For purposes of this Section 9, the following definitions shall apply.

“Conflict of Interest in Research Official” or **“COIR Official”** means the individual designated by H+H to solicit and review disclosures of Significant Financial Interests from each Covered Individual who is planning to participate in, or is participating in, Research.

“Conflict of Interest in Research Committee” or **“COIR Committee”** means the institutional body designated by H+H that is responsible for determining and reporting Financial Conflicts of Interest defined in this Policy.

“Covered Individual” means Principal Investigators, Sub-investigators, collaborators, consultants and other key Research personnel responsible for the design, conduct, or reporting of the Research.

“Disclosure of Significant Financial Interests” means a Covered Individual’s disclosure of Significant Financial Interests to H+H.

“Equity Interest” means any stock, stock option, or other ownership interest (as determined through reference to public prices or other reasonable measures of fair market value, if the interest involves a publicly traded company).

“Financial Conflict of Interest” or **“FCOI”** means a Significant Financial Interest that could directly and significantly affect the design, conduct, or reporting of PHS-funded research.

“FCOI Report” means H+H’s report of a Financial Conflict of Interest to a PHS Awarding Component.

“Financial Interest” means anything of monetary value, whether or not the value is readily ascertainable.

“Institutional Responsibilities” means a Covered Individual’s professional responsibilities on behalf of H+H which include, but are not limited to, Research, Research consultation, teaching, professional practice, H+H committee memberships, and service on panels such as Institutional Review Boards or Data and Safety Monitoring Boards.

“Manage” means taking action to address a Financial Conflict of Interest, which can include reducing or eliminating the Financial Conflict of Interest, to ensure, to the extent possible, that the design, conduct, and reporting of Research will be free from bias.

“PHS” means the Public Health Service of DHHS and any components of the PHS to which the authority involved may be delegated, including the NIH.

“PHS Awarding Component” means the organizational unit of the PHS that funds the Research that is subject to this Policy.

“Remuneration” means salary and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship).

“Senior/Key Personnel” means the Principal Investigator and any other personnel considered to be essential to work performance in accordance with DHHS’ acquisition regulations (“HHSAR”) subpart 352.242-70 and identified as key personnel in the contract proposal and contract.

“Significant Financial Interests” or **“SFIs”** mean those interests that Covered Individuals must disclose to H+H pursuant to Section 9.3.4(a) of this Section.

“Subrecipient” means an entity, including a subcontractor or consortium member that carries out Grant-funded Research on behalf of H+H.

9.3 Procedures

9.3.1 H+H in its discretion may delegate COI review to a reviewing IRB, in which case the designated reviewing IRB will be responsible for reviewing all potential COIs for all study personnel. If a significant COI exists, a management plan will be established by the Office of Research Administration or the IRB.

9.3.2 If the designated IRB cannot review potential COIs, H+H will review all potential COIs according to Section 9.3.3.

9.3.3 Designation of Responsible Parties; Responsibilities.

(a) *Conflicts of Interest in Research Official.* H+H shall appoint a Conflicts of Interest in Research Official (“COIR Official”) and shall communicate and/or make readily available the COIR Official’s contact information to all Principal Investigators.

(b) *COIR Committee.*

(1) H+H shall form an H+H-wide standing Conflict of Interest in Research Committee (“COIR Committee”). The members will be chosen by the Executive Director, H+H Office of Legal Affairs, Office of Corporate Compliance, and Office of Research Administration, who shall also determine the members’ respective term limits.

(2) COIR Committee shall include (i) H+H’s COIR Official and other officials experienced in the oversight of conflicts of interest and familiar with applicable laws and regulations, (ii) one Principal Investigator from each network of Facilities (Manhattan, Bronx, Brooklyn, Staten Island and Queens), (iii) the RA Director, and (iv) any other individuals who conduct Human Subjects Research at H+H, as necessary.

(c) *Responsibilities.*

(i) The COIR Official shall be responsible for:

(1) Soliciting and reviewing disclosures of Significant Financial Interests of Covered Individuals related to their Institutional Responsibilities.

(2) Reasonably determining whether a conflict of interest in Research exists.

(3) Serving as a member of the COIR Committee.

(ii) The COIR Committee shall be responsible for:

(1) Reviewing any request by a Covered Individual to rebut the presumption that he or she may not conduct Research.

(2) Documenting the COIR Committee's findings and the bases for any recommendation to permit or to recommend against permitting Covered Individuals to conduct Research in relation to their disclosed financial interests.

(3) Managing and overseeing when Covered Individuals are permitted to conduct Research in relation to their disclosed financial interests.

(4) Communicating to responsible H+H officials information regarding Significant Financial Interest in a Research Project, and the COIR Committee's findings and recommendations regarding the management of conflicts. To the extent the Covered Individual has not notified the applicable IRB about the underlying Significant Financial Interest, the COIR Committee shall also notify that IRB.

(5) Maintaining a quorum of 51% for required meetings, which can be accomplished by physical presence or teleconference. Each member shall vote by ballot.

(iii) The RA Director shall be responsible for reviewing any FCOI referred by the COIR Committee to determine whether the FCOI can be managed such to allow Research Project to proceed, as described in Section 9.3.6(b)(i)(4).

(iv) The Office of Research Administration shall be responsible for:

(1) Providing to the COIR Official any SFI Disclosure Forms received from a researcher during the Research approval process.

(2) Providing reminders to researchers prior to the due date of any annual SFI Disclosure Form, as described in Section 9.3.4(a)(i).

(v) Covered Individuals shall be responsible for:

(1) Disclosing their Significant Financial Interests, or those of their spouses or dependent children, as required under Section 9.3.4.

(2) Complying with the SFI review process as set forth in Section 9.3.6

(3) Completing training as required under Section 9.3.9.

9.3.4 Disclosure of Significant Financial Interests.

(a) *Initial and Annual Disclosures.*

(i) Covered Individuals must disclose certain financial interests and non-H+H obligations, as well as those of their immediate family (i.e., spouse and dependent children) by completing and submitting to the COIR Official a completed Conflict of Interest Form, Disclosure of Significant Financial Interests and Obligations (the “SFI Disclosure Form”) (**Exhibit 9**). The SFI Disclosure Form must be completed and submitted by the Covered Individual to the Office of Research Administration with each application or proposal submitted for funding, and annually during the period of any award or contract. The Office of Research Administration will provide reminders to researchers prior to the due date of any annual SFI Disclosure Form.

(ii) The following Significant Financial Interests of the Covered Individual or his/her immediate family must be disclosed in the SFI Disclosure Form:

(1) Remuneration received from or Equity Interest in a publicly traded company related to the Covered Individual’s Institutional Responsibilities of any value and from any source, if the aggregated value of the Remuneration or Equity Interest in the twelve months preceding the disclosure exceeds \$5,000;

(2) Remuneration received from a non-publicly traded company related to the Covered Individual’s Institutional Responsibilities of any value and from any source, if the aggregated value in the twelve months preceding the disclosure exceeds \$5,000;

(3) Any Equity Interest in a non-publicly traded company related to the Covered Individual’s Institutional Responsibilities held by a Covered Individual or his/her immediate family;

(4) Intellectual property rights and interests, including, but not limited to, patent, trademarks, copyrights or licensing

agreements, upon receipt of income related to such rights and interests;

(5) Membership on any independent scientific advisory board, if the value of any Remuneration received for service on such board in the twelve months preceding the disclosure exceeds \$5,000;

(6) The occurrence of any reimbursed or sponsored travel (i.e., that which is paid on behalf of the Covered Individual and not reimbursed to the Covered Individual so that the exact monetary value may not be readily available), related to his/her Institutional Responsibilities.

a. The Covered Individual must disclose the following related to travel: (i) the purpose of the trip; (i) the identity of the sponsor/organizer; (iii) the destination; (iv) the duration of the trip; and (v) any further information as required by the COIR Official.

b. Excluded from this category are travel expenses which are reimbursed by a Grant or Sponsor contract.

(7) In the case of the annual submission of the SFI Disclosure Form, any updated information regarding any previously disclosed Significant Financial Interest (e.g., the updated value of a previously disclosed equity interest).

(b) *Event-Based Disclosure.* Covered Individuals must submit an updated SFI Disclosure Form as follows:

(i) Immediately upon discovery of any SFI that was inaccurately reported or omitted from a previously submitted SFI Disclosure Form;

(ii) Within thirty (30) days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new Significant Financial Interest; and

(iii) Upon the transfer of a Research Project from another institution.

(c) *Affiliate Disclosure.* A Covered Individual employed by an Affiliate who completes a conflicts of interest disclosure form as required by the applicable IRB or pursuant to a similar conflicts of interest policy of the Affiliate may submit such form to the COIR Official for an exemption from the disclosure requirements of this Section. The COIR Official will review the disclosure form to ensure it is

sufficient to meet the requirements of this Section and may require the Covered Individual to provide additional information.

9.3.5 Subrecipient Requirements. Where Research is carried out through a Subrecipient, H+H and the Subrecipient must comply with the following:

(a) *Written Agreement.* H+H and the Subrecipient must establish in a written agreement whether this Section 9 or the financial conflicts of interest policy of the Subrecipient will apply to the Subrecipient's investigators.

(b) *Application of Subrecipient Policy.* If the Subrecipient's investigators must comply with the Subrecipient's financial conflicts of interest policy, the agreement referenced above must:

(i) Contain a certification by the Subrecipient that its policy complies with all Federal and State laws and regulations, including, but not limited to, 42 C.F.R. Part 50 Subpart F and 45 C.F.R. Part 94; and

(ii) Specify time period(s) for the Subrecipient to report all identified financial conflicts of interest to H+H sufficient to enable H+H to provide timely FCOI Reports, as necessary, to governmental agencies as required by Federal and State law and regulations.

(c) *Application of H+H Policy.* If the Subrecipient's investigators must comply with this Section 9, the agreement referenced above shall specify time period(s) for the Subrecipient to submit all investigator disclosures of Significant Financial Interests to H+H sufficient to enable H+H to comply timely with its review, management, and reporting obligations as required by Federal and State law and regulations and this Section.

9.3.6 Review and Management of FCOIs.

(a) *Guidelines for Determining FCOIs.* A Significant Financial Interest shall be deemed to be a Financial Conflict of Interest where:

(i) It is determined, in consultation with the Covered Individual at the discretion of the COIR Official or COIR Committee, that the Significant Financial Interest is related to PHS-funded Research. A SFI is related to PHS-funded Research when it is reasonably determined that the SFI:

(1) Could be affected by the Federally-funded Research;
or

(2) Is in an entity whose financial interest could be affected by the Research; and

(ii) The COIR Official or COIR Committee, as applicable, reasonably determines that the SFI could directly and significantly affect the design, conduct, or reporting of the Federally-funded Research.

(b) *Review Procedure for Financial Interests.*

(i) Review Prior to Expenditures of Funds for New Research Projects. The following SFI review procedures must occur prior to the expenditure of any award or contract funds:

(1) Preliminary Review. Covered Individuals shall submit an SFI Disclosure Form with each proposal submitted for funding to the Office of Research Administration. The Office of Research Administration will forward the SFI Disclosure Form to the COIR Official for an initial review as to whether any disclosed SFI constitutes a FCOI.

(2) Expedited Review. In instances where the SFI is minimal (less than \$5,000 per year) and/or only requires a straight-forward and modest plan to reduce, eliminate or manage the potential conflict, the COIR Official may elect to conduct an expedited review and approval. Such approval is reported to the entire COIR Committee on a quarterly basis.

(3) Full Review; COIR Committee Review. Where the magnitude of the SFI is unclear, or the SFI is not minimal, the COIR Committee will conduct a full review to determine whether a FCOI exists. The COIR Committee will prepare an information packet for review by the RA Director.

(4) RA Director Review. Based on the information provided by the COIR Committee, the RA Director may either allow Research to proceed with elimination or management of the FCOI, or suspend Research until such FCOI can be managed appropriately.

a. *Research Project Proceeds.* If the RA Director recommends that the Research proceed, a plan for management or elimination of any conflicts shall be prepared by the RA Director in collaboration with the COIR Official and COIR Committee.

b. *Suspension of Research Project.* In cases where H+H determines that it cannot manage the conflict, it may require that the conflict be eliminated or that the Research not proceed. Factors in this decision might include the involvement of Human Subjects in the Research Project, the level of risk involved, the nature and significance of the conflict, the potential for having a serious adverse impact on

the scientific field or on the reputation of H+H, and the level of difficulty involved in managing the conflict relative to the benefit of the Research Project.

(5) Prospective Management Plan. An approved plan for management or elimination of the conflict of interest must be in place before the Research begins. Federal grant applications may be submitted while H+H is considering a possible conflict of interest with the understanding that H+H will not approve the Research Project unless the conflict can be managed or eliminated. H+H shall notify the applicable PHS Awarding Component of the possible conflict of interest and work with the PHS Awarding Component to expeditiously resolve the conflict of interest concerns.

(c) *Review of SFIs Disclosed After Commencement of Research.*

(i) New Disclosures for Ongoing Research Projects. Where a Covered Individual submits an initial SFI Disclosure Form related to any ongoing Research Project (i.e. a Research Project transferred from another institution, or the Covered Individual is new to a Research Project), the COIR Official shall, within sixty (60) days of the disclosure determine whether a Financial Conflict of Interest exists; and, if so, implement, on at least an interim basis, a management plan, as set forth in Section 9.3.6(d).

(ii) Review of SFIs not Timely Disclosed. Whenever H+H identifies a Significant Financial Interest that was not disclosed in a timely manner by a Covered Individual or, for whatever reason, was not previously reviewed by the COIR Official during an ongoing PHS-funded Research Project (e.g., was not timely reviewed or reported by a Subrecipient), the COIR Official shall:

(1) Within sixty (60) days of discovery of the SFI determine whether a Financial Conflict of Interest exists; and, if so:

(2) Implement, on at least an interim basis, a management plan as set forth in Section 9.3.6(d); and

(3) Conduct a retrospective review, as described below in Section 9.3.6(c)(iii).

(iii) Retrospective Review.

(1) A retrospective review to determine whether a FCOI resulted in bias in the design, conduct or reporting of the Research Project during the time of noncompliance must be conducted by the COIR Committee within 120 days of discovery of any of the following circumstances:

a. A failure by the Covered Individual to disclose a Significant Financial Interest that is determined by H+H to constitute a Financial Conflict of Interest;

b. Failure by H+H to review or manage such a Financial Conflict of Interest;

c. Failure by the Covered Individual to comply with a Financial Conflict of Interest management plan; or

d. Any other failure to comply with these procedures.

(2) H+H will document the retrospective review in a retrospective review report that shall include all elements and information required by law and regulation.

(3) Based on the results of the retrospective review, if appropriate, H+H shall update any other reports submitted to any PHS Awarding Component specifying the actions that will be taken to manage the Financial Conflict of Interest going forward. If a retrospective review reveals bias, H+H will notify the PHS Awarding Component promptly and submit a Mitigation Report to the PHS Awarding Component, as described in Section 9.3.7(b).

(d) *Management Plan for the Conflicts of Interest.*

(i) If it is determined through the above review procedures that an SFI is a FCOI, the COIR Committee, in consultation with the Principal Investigator, must create a management plan to manage, reduce, or eliminate any FCOI. Specific management methods in handling individual FCOIs include, but are not limited to:

(1) Full disclosure to any Human Subjects of the Covered Individual's FCOI.

(2) Disclosure of the Covered Individual's FCOIs in all written and oral presentations, publications, and abstracts.

(3) Modification of the Research Project Protocol, including changing the site(s) of the Research Project.

(4) Monitoring of Research by independent reviewers.

(5) Divestiture of Significant Financial Interests.

(6) Severance of relationships that create actual or potential conflicts.

(7) Disqualification of the Covered Individual from part or all of the Research Project.

(ii) Once a management plan is in place, it will be reviewed on an ongoing basis until the completion of the PHS-funded Research Project. The Covered Individual must inform the COIR Committee of any changes in the SFI.

(iii) Such management plan will be given to the applicable IRB which may request other mitigation actions in addition to those contemplated in the management plan.

(e) *Covered Individual Acknowledgement of FCOI Determination.* If the COIR Official, COIR Committee or RA Director determines that a Financial Conflict of Interest exists, copies of the final decision will be sent to the Covered Individual, Chair of the Covered Individual's department, and the responsible Institutional Review Board. Upon receipt of the decision, the Covered Individual must either acknowledge it or submit an appeal. Funding will be held until the Covered Individual agrees to comply with the management plan.

(f) *Appeal of FCOI Determination.* The Covered Individual has ten (10) days from receipt of the determination to submit an appeal in writing to the RA Director. The appeal should include the specific provisions being challenged, the reason for the appeal, and the justification for a different outcome. The Covered Individual may also provide an alternative management plan and any supplemental information that might be helpful to the RA Director in making a final determination. This decision shall be final and not further appealable.

9.3.7 H+H Reporting Requirements to NIH.

(a) *FCOI Reports.*

(i) Initial FCOI Report. Prior to H+H's expenditure of any funds under a PHS-funded Research Project, H+H shall provide to the PHS Awarding Component an FCOI Report regarding any FCOI and ensure that H+H has implemented a management plan in accordance with Section 9.3.6(d). In cases in which H+H identifies a FCOI and eliminates it prior to the expenditure of PHS-awarded or contracted funds, no FCOI report is required.

(ii) Annual FCOI Reports. For any FCOIs previously reported by H+H with regard to an ongoing PHS-funded Research Project, H+H will provide to the PHS Awarding Component an annual FCOI Report that addresses the status of the FCOI and any changes to the management plan for the duration of the PHS-funded Research Project (including extensions with or without funds) in the time and manner specified by the PHS Awarding Component.

(iii) New Researchers or Transferred Research Projects. For any FCOI identified during an ongoing PHS-funded Research Project (e.g., upon the participation of a Covered Individual who is new to the Research Project or upon transfer of a Research Project from another institution), H+H shall provide within sixty (60) days to the PHS Awarding Component a FCOI Report ensuring that H+H has implemented a management plan in accordance with Section 9.3.6(d).

(iv) Report Contents. All FCOI reports required under this Section 9.3.7(a) shall include sufficient information to enable the PHS Awarding Component to understand the nature and extent of the Financial Conflict of Interest, and to assess the appropriateness of H+H's management plan or other mitigation efforts, as well as all elements and information required under applicable law and regulation.

(b) *Mitigation Reports.* For FCOIs resulting from SFIs that were not timely disclosed or reviewed (as discussed in Section 9.3.6(c)(ii)) H+H must provide to the Research Project's PHS Awarding Component a Mitigation Report if it is determined in its retrospective review discussed in Section 9.3.6(c)(iii) that the FCOI resulted in bias in the design, conduct or reporting of the Research Project during the time of noncompliance. The Mitigation Report shall document the key elements of the retrospective review and the impact of the bias on the Research Project, and all other information required under applicable law and regulation.

(c) *Notification of Corrective Actions.* If a Covered Individual fails to comply with this Policy or a Financial Conflict of Interest management plan, and such failure appears to have biased the design, conduct, or reporting of the PHS-funded Research, H+H will promptly notify the PHS Awarding Component of the corrective action taken or to be taken.

(d) *Submission Procedure.* H+H will submit FCOI Reports via the electronic Research Administration (eRA) Commons FCOI Module and other reports and notifications as required by the PHS Awarding Component.

9.3.8 Maintenance of Records. The RA Director will maintain records relating to all disclosures by Covered Individuals of financial interests, including those submitted to an Affiliate, and H+H's review of, and response to, such disclosures (whether or not a disclosure resulted in a determination of a Financial Conflict of Interest) and all actions, including corrective action plans, under H+H's policy or retrospective review, if applicable, as follows:

(a) *PHS Grant or Cooperative Agreement.* In the case of Research Projects for which funding was obtained through a PHS Grant or a PHS cooperative agreement, the later of:

(i) For three (3) years from the date of the submission of the final expenditures report to the PHS, or

(ii) Where applicable, for the time periods specified in 45 C.F.R. §§ 74.53(b) and 92.42 (b) for different situations.

(b) *PHS Contract.* In the case of Research Projects for which funding was obtained through a contract with PHS for property or services for the direct benefit of the Federal government, the later of:

(i) For three years from the date of final payment, or

(ii) Where applicable, for the time periods specified in 48 C.F.R. Part 4, subpart 4.7.

9.3.9 Training.

(a) *Initial Training.* H+H will inform Covered Individuals of this policy, their responsibilities under this policy, and the applicable Federal regulations by providing each Covered Individual, at the commencement of each Research Project, with a copy of this policy by e-mail/in paper form. H+H requires each Covered Individual to complete training regarding conflicts of interest and the disclosure requirements under this Section prior to engaging in Research, regardless of funding source.

(b) *Additional Training.* Researchers are required to participate in additional training with regard to their responsibilities under this Section at least every two years, and immediately when any of the following circumstances apply:

(i) H+H revises its financial conflict of interest policies or procedures in any manner that affects the requirements of Covered Individuals;

(ii) A Covered Individual is new to H+H; or

(iii) H+H finds that a Covered Individual is not in compliance with H+H's Financial Conflict of Interest in Research policy or management plan.

(c) *Education Tracking.* The Office of Research Administration will track fulfillment of training requirements and will maintain records of completion dates.

9.3.10 Enforcement Mechanisms, Remedies and Noncompliance.

(a) *Enforcement.* All Covered Individuals must comply with this FCOI in Research Policy. Breach of this Policy shall include but is not limited to the individuals' failure to disclose an SFI, untimely disclosure of an SFI, and failure to abide by any FCOI management plan imposed by the COIR Committee. Individuals who engage in such breach shall be disciplined in accordance with H+H's Employee Disciplinary Policy and/or Medical Staff By-Laws.

(b) *FCOIs in drug, medical device or treatment efficacy studies.* In any case in which DHHS determines that a PHS-funded Research Project intended to evaluate the safety or effectiveness of a medical product or treatment has been designed, conducted, or reported by Covered Individual with a Financial Conflict of Interest that was not managed or reported by H+H as required by this Section, H+H shall require the Covered Individual involved to:

(i) Disclose the Financial Conflict of Interest in each public presentation of the results of the Research, and

(ii) To request an addendum to previously published presentations.

9.3.11 Public Accessibility.

(a) *Public Access to this FCOI Policy.* H+H will make this Financial Conflicts of Interest in Research Policy accessible via its publicly accessible Web site.

(b) *Public Accessibility to Information regarding Reported FCOIs.*

(i) Interests to be Posted. Prior to H+H's expenditure of any funds under a PHS-funded Research Project, H+H will post on its Web site, and update for the duration of the Research Project, information concerning any FCOI in accordance with applicable law and regulations.

SECTION 10. PUBLICATIONS

10.1 Policy

H+H requires the dissemination of Research knowledge in the public interest. If this Research knowledge is acquired in work involving Human Subjects at H+H and/or using H+H resources, and is disseminated through publications, abstracts, presentations, or posters, H+H is required to be acknowledged per the guidelines listed below. H+H and its employees have a responsibility to ensure that H+H receives proper credit for Research in articles, presentations, interviews, and other professional activities in which the results of that Research are publicized or recognized.

All types of documentations listed above are required to be submitted to the Office of Research Administration for archival purposes.

All negotiated agreements governing collaboration on a Research Project should include a "Publications" section. Please see **Exhibit 5** for details.

If the journal does not specify guidelines for authorship, citations or acknowledgements, please use the procedures below.

10.2 Procedure

H+H has established the following requirements regarding notification of pending publications and presentations:

10.2.1 Notification Process.

(a) Principal Investigator shall notify the Office of Research Administration as soon as an article is accepted for publication. This applies to all publications based on Research, regardless of funding source. Early notification allows H+H to prepare briefing materials for H+H leadership and plan for other dissemination.

(b) The Principal Investigator shall provide the Office of Research Administration with a copy of any material it intends to publish or publicly communicate at least thirty (30) days in advance of when it intends to publish or publicly communicate, so that H+H has a sufficient opportunity to provide comments. The Principal Investigator is required to consider H+H's comments in good faith.

(c) H+H will strictly adhere to embargoes put in place by the journals and will notify the Principal Investigator before issuing any press release or publication regarding the respective Research Project. Once published, H+H may highlight important findings in a variety of print and electronic publications. To ensure accuracy in reporting, no press release should be disseminated without approval of the author.

10.2.2 Attribution and Acknowledgement of H+H Research Support/Resources/Employment.

(a) *H+H Research Support.* All publications and presentations of H+H Research results must contain the following (or equivalent) acknowledgement, if permitted by the journal:

(i) If H+H provided direct Research funding, the publications or presentations must contain the following acknowledgment: "This material is based upon work supported (or supported in part) by the New York City Health and Hospitals Corporation."

(ii) If H+H provided no direct Research funding, but the Research involved the use of other H+H resources (e.g., H+H Facilities or patients), the publications, or presentations must contain an acknowledgement of H+H or the Facility. If Principal Investigator cannot acknowledge H+H for any reason, the Principal Investigator must notify the Office of Research Administration in advance of publication and must cooperate with the Office of Research Administration to attempt to have H+H acknowledged.

(b) *Acknowledgement of H+H Affiliations.* Authors of clinical and Research publications, abstracts, and presentations must acknowledge their affiliation using the following format, if permitted by the journal: “H+H Department, H+H Facility” (for example, “Department of Pediatrics, Jacobi Medical Center, Albert Einstein College of Medicine”). If multiple Facilities were involved in the Research, the author may reference H+H generally, as permitted by the journal.

(i) When the Principal Investigator has a majority H+H appointment, H+H must be named first, regardless whether H+H is the primary source of funding or where the funds are administered.

(ii) Authors or presenters of Research results are required to list H+H employment first if any of the following conditions apply:

(1) The Research was funded primarily from H+H resources (50 percent or more), either directly or indirectly;

(2) The Research was conducted primarily in H+H Facilities; or

(3) The first author was a junior scientist (e.g., resident, trainee) whose salary may not have been provided by H+H, but who primarily used H+H funding or Facilities, or whose mentor or supervisor was primarily employed or funded by H+H.

(c) *Research Funded by a Sponsor or Grantor.* Principal Investigator is responsible for informing Sponsors and Grantors of his or her obligation to acknowledge, in all Research publications, the cooperation and support provided by H+H and each Facility, when such has occurred. The Office of Research Administration has discretion to disapprove of any agreement with a Sponsor or Grantor that does not contain appropriate acknowledgment language.

10.2.3 License. H+H shall have a royalty-free, non-exclusive and irrevocable license to reproduce any material or publications involving H+H Research.

10.2.4 Registering a study at ClinicalTrials.gov.

(a) In order to comply with the [Final Rule for Clinical Trials Registration and Results Information Submission](#) in accordance with Section 801 of the Food and Drug Administration Amendments Act (FDAAA 801), and the [NIH Policy on the Dissemination of NIH-funded Clinical Trial Information](#), Research that involves drugs, devices, or biologics that are regulated by the FDA and all Research that is funded in whole or in part by the NIH and meets the NIH’s definition of a clinical trial must be registered at ClinicalTrials.gov within 21 days of enrolling the first subject.⁸⁸ [Section 801 of the Food and Drug Administration Amendments Act \(FDAAA 801\)](#) (PDF) requires responsible parties to register clinical trials and submit summary results to ClinicalTrials.gov.

(b) Further, the International Committee of Medical Journal Editors (ICMJE) requires trial registration as a condition of the publication of research results generated by a clinical trial. To fulfill this obligation organizations and individuals can provide the World Health Organization (WHO) Trial Registration Data Set required by ICMJE to ClinicalTrials.gov or a WHO primary registry. The ICMJE expects authors to meet all results reporting requirements of their funding and regulatory agencies. If there are no such reporting requirements, the ICMJE encourages authors to submit results information to the same database on which their trials are registered.

SECTION 11. INVENTIONS

11.1 Policy

It is the intent of H+H to administer intellectual property rights for the public benefit, and to encourage and assist members of the faculty, staff, and others associated with H+H in the use of the patent system with respect to their Inventions in a manner that is equitable to all parties involved. This Section governs the handling of Inventions made by individuals involved in educational, Research, clinical and other activities at Facilities.

H+H recognizes the need for and desirability of encouraging the broad utilization of the results of Research, not only by scholars but also in practical application for the general public benefit, and acknowledges the importance of the patent system in bringing innovative Research findings to practical application.

Except as otherwise provided in this Section, and in compliance with New York Public Officers Law § 64-A on patents, Inventions that are conceived, reduced to practice or developed by members of the Research Team are solely owned by H+H, and no other person or entity shall have any rights of ownership or interest in such Inventions, if conceived, reduced to practice or developed, in whole or part: (1) in the scope of H+H employment or other duties at or on behalf of H+H, whether as an Affiliate or otherwise; (2) in connection with Research or clinical activities at or under the auspices of H+H; (3) with substantial use of H+H resources; (4) the Invention is subject to the rights of a Grantor or Sponsor or other third parties under agreements duly entered into or agreed to by H+H. Any and all exceptions to this policy shall be determined and approved by the President of H+H in consultation with the Intellectual Property Committee (IPC) and Office of Legal Affairs.

It is the policy of H+H to advise the Inventor within a reasonable period of time following disclosure of his or her Invention to the Office of Research Administration in writing whether rights of ownership to the Invention will be retained by H+H or released to the Inventor, or to a third party if so obligated by a Contract or Grant.

11.2 Definitions

For purposes of this Section 11, the following definitions shall apply.

“Covered IP” means all intellectual property rights, including all patent, trademark, copyright and trade secret rights (as defined in the Uniform Trade Secrets Act) in all subject matters created, conceived of or reduced to practice or writing or first fixed in a tangible medium of expression in the course of or as a direct result of Research hereunder, including but not limited to such rights in inventions or innovations (whether or not patentable), in all copyright and copyrightable material (unless published in academic or scholarly media or otherwise in the public domain), and all such intellectual property rights inhering in tangible research property such as cell lines, vectors, other biological and agricultural materials, therapeutic agents or pharmaceuticals, medical devices, biological and agricultural materials, therapeutic agents or integrated circuit chips, computer databases and prototype devices, improvements, modifications thereon domestic and foreign, including all continuations, provisionals and divisionals thereof and all applications, registrations and renewals of the foregoing. For the avoidance of doubt, and without limitation, “Covered IP” excludes (a) pre-existing intellectual property; and (b) tangible property of a party to the extent that such tangible property involves only the realization of pre-existing intellectual property and involves de minimus inventive or original effort.

“Equity” means shares of stock or other securities issued by the licensee or another corporation.

“Invention” means Covered IP that is created, conceived of or reduced to practice or writing or first fixed in a tangible medium of expression in the course of or as a result of Research.

“Inventor” means the member(s) of the Research Team who makes an Invention.

“Net Royalties” means income from Royalties after allocation of the first monies to the payment of any and all fees and costs, including legal counsel fees incurred by H+H in obtaining any patent protection for an Invention.

“Royalties” means running royalties, advances against running royalties, up-front license fees, milestone payments, Equity, and any other payments received by H+H under a license agreement in consideration for licensing an Invention, but shall not include amounts received from a licensee or others in sponsorship of Research or under other agreements for other goods, services or rights.

11.3 Procedure

11.3.1 Disclosure and Filing.

(a) *Disclosure.* All H+H employees and staff shall promptly disclose all Inventions to the Office of Research Administration using the Inventions Disclosure Form, attached as **Exhibit 10**. Upon receipt of the completed Inventions Disclosure Form, the Office of Research Administration will:

(i) In its discretion, meet with the Inventor to evaluate the Inventions Disclosure Form;

(ii) Forward the Inventions Disclosure Form to the Intellectual Property Committee described in Section 11.3.3 below; and

(iii) If the Research Project is supported by government funds, promptly and fully report such Invention to the funding agency for determination as to whether patent protection of such Invention shall be sought and how the rights in the invention or discovery, including rights under any patent issued thereon, shall be disposed of and administered in order to protect the public interest.

(b) *Filing.* Subject to the rights of the government and any agreements with non-governmental entities into which H+H has entered, H+H shall have authority to manage the process of (a) the filing, prosecution and maintenance of copyright applications and registrations, patent applications and patents, registrations and other protective measures; (b) licensing, assignment, joint-venturing or other commercial opportunities; and (c) all agreements and all measures to commercialize or realize the value or benefit of an Invention. H+H shall use reasonable efforts to successfully commercialize such Invention.

11.3.2 Confidential Information. As a condition of employment/appointment with H+H, employees/staff shall hold in strictest confidence any confidential information, which includes any of H+H's propriety information, technical and clinical data, trade secrets or know-how, including, but not limited to, medical and scientific research, analysis systems, procedures, tests, software, developments, Inventions, processes, formulas, technology, designs, drawings, engineering, hardware configuration information, or business information disclosed to the employee/staff by H+H either directly or indirectly in writing, orally, by drawing or observation of parts of equipment.

11.3.3 Intellectual Property Committee.

(a) *Committee Formation.*

(i) The Intellectual Property Committee (IPC) is a committee that will meet to respond to an Invention disclosure, copyright concerns, and trademarks managed by H+H. IPC members and the IPC Chair are chosen by the President and serve at his/her discretion. The IPC will have a minimum of four (4) members, including the IPC Chair and shall include the following:

- (1) Internal (H+H) physician scientist with expertise in the area;
- (2) A representative from the Office of Legal Affairs;
- (3) Business and financial advisor, chosen at the discretion of the President; and
- (4) An external advisor in the therapeutic area, chosen at the discretion of the President.

(ii) If applicable, an Affiliate, Grantor or Sponsor representative should be included on the IPC where an Invention implicates the rights of those entities.

(b) *IPC Review of Invention Disclosures.*

(i) Upon receipt of a completed Inventions Disclosure Form from the Office of Research Administration, the IPC will review the disclosure within ninety (90) days.

(ii) Upon the review of the disclosure, the IPC will recommend the appropriate next steps of 1) recommending not to pursue a patent and releasing the Inventor of H+H's interests, 2) recommending to H+H that it provide funding for patent searches, IP applications, lawyers, and other expenses required to pursue a patent, copyright, or trademark, or 3) seeking additional guidance from an external source with respect to H+H's or other third party's interests in such Inventions.

(iii) If the IPC decides that it does not wish, and has no legal obligation to participate in the patenting or licensing of an Invention, the IPC may release to the Inventor H+H's interest in the Invention, and the Inventor shall then be free to dispose of the Invention as he or she wishes.

(iv) All rights to and interests in Inventions arising in the course of Research sponsored by H+H, any government or private company, or other sponsored research are controlled by the terms of the applicable research agreement.

(c) *Recommendations on Disbursements.* The IPC will assist with the recommendation of the applicable distribution formula and oversight of the disbursement of revenues.

11.3.4 Rights and Obligations of the Parties.

(a) *Inventor(s) Rights.*

(i) Multiple Inventors. The term "Inventor" may represent two or more individuals. These individuals will be expected to agree among themselves on the fractional distribution of the "Inventor" share of any Royalties. A written agreement must be signed by all the individuals involved, and retained for the record with the IPC. If no such agreement exists at the time of a distribution of Net Royalties, the Inventors' share of such distribution shall be divided equally among the Inventors.

(ii) The Inventor(s) has the right to:

(1) Receive notice within a reasonable time of H+H's intention to file a patent application or otherwise to retain title to the Invention after disclosure to H+H of an Invention.

(2) Receive an equitable share of any licensing fees or Royalties received by H+H from the commercialization of the Invention according to the distribution of proceeds;

(3) Receive from H+H title to any Invention subject to this Policy in the event H+H elects not to retain title; and

(4) Publish their research findings in a timely manner (no more than 90 days) after the submission of a patent application.

(b) *Inventor Obligations.* The Inventor(s) is obligated to:

(i) Upon discovery that he or she may have developed H+H-owned Invention, report promptly to the H+H IPC through the Invention Disclosure Form a summary of the concepts, relevant data, observations and general claims with respect to any Inventions well as the name(s) of any collaborator(s);

(ii) Assign right, title, and interest to the Invention to H+H;

(iii) Inform Affiliates if an Invention is a result from an Inventor with joint appointments and the Research Project is funded by both H+H and Affiliate resources;

(iv) Cooperate to the extent necessary as determined by H+H in:

(1) Reasonably delaying of publication to allow for submission of a patent application;

(2) Prosecuting all patent applications and other required documents;

(3) Participating in the defense of such patents during prosecution for interference or infringement;

(v) Keep and maintain adequate and current written records of all Inventions;

(vi) Grant H+H a nonexclusive, royalty-free, irrevocable, perpetual worldwide license to Inventions for research, educational, legal, regulatory, reporting, IRB, patient/public safety and charitable purposes and to comply with any law or regulation; and

(vii) Assist with licensing or marketing efforts related to the Invention.

(c) *H+H Obligations.* H+H is obligated to:

(i) Assign to the Inventor title to any Invention subject to this Section for which H+H chooses not to retain title;

(ii) Make, use, license, assign or sell to a third party the rights and interests of any patented or unpatented Invention owned by H+H, and exclude others from doing so;

(iii) Make Principal Investigators and Research Staff aware of this Section and of any ongoing agreements with external sources to evaluate and/or market such Inventions;

(iv) Inform Affiliates if an Invention has been disclosed by an Inventor with joint appointments and the Research Project is funded by both H+H and Affiliate resources;

(v) After an Invention is disclosed, act in a timely fashion to determine whether H+H and/or Affiliate choose to retain title, to submit to an external source for evaluation, and/or determine whether a patent application is to be filed;

(vi) Give notice to an Inventor, within a reasonable time after disclosure of an Invention, of H+H's decision to file a patent application or otherwise retain title to the Invention;

(vii) Expedite intellectual property protection so as to minimize the delay of publication, no more than ninety (90) days after the submission of the patent application; and

(viii) Distribute licensing fees or Royalties received by H+H for any Invention according to the distribution of proceeds described in Section 11.3.6.

11.3.5 Licensing. H+H may, in some circumstances with due consideration to the perspective licensee and when consistent with law applicable to Federally supported Research, license a patented Invention on an exclusive or nonexclusive basis for a reasonable period up to the full term of the patent, provided that such license shall contain provisions to promote the likelihood that the Invention provides a public benefit, such as a requirement of due diligence and march-in rights when the licensee does not adequately perform. H+H also may elect to license unpatented technology on an exclusive or nonexclusive basis.

11.3.6 Distribution of Proceeds.

(a) In the event that income is realized, H+H shall allocate the first monies to the payment of any and all fees and costs, including legal counsel fees incurred by H+H in obtaining any patent protection.

(b) After this deduction by H+H, a separate agreement with the Inventor shall be negotiated to share the Net Royalties to be equitably distributed with 1) Inventor; 2) Division/Lab/Research program; 3) H+H to be primarily used to further pursuit of Research activities.

(c) Net Royalties shares will be distributed twice per year, in July and January based on revenues from the prior half fiscal year.

PART III

CONTINUING APPROVAL, CONCLUSION & MONITORING OF ONGOING RESEARCH PROJECTS

SECTION 12. H+H CONTINUING APPROVAL

12.1 Policy

In order to fulfill the assurances given to the Federal government by H+H under its FWA during the course of a Research Project for which initial approval has been obtained under Section 4, Facilities must regularly review the progress and safety of the Research Project and Principal Investigators must request continuing approval of the Research Project in accordance with the procedure below.

12.2 Procedures

12.2.1 Applying for Continuing Approval. The Principal Investigator will apply for continuing approval in STAR. A complete Continuing Approval application includes an IRB Progress Report, when applicable, and continuing review approval from the IRB, when applicable. These documents should be submitted to STAR prior to the H+H expiration date, which is equivalent to the IRB date of expiration listed in STAR.

12.2.2 Facility and H+H Central Office Approval for Continuation of Research. If there have been no Major Protocol Violations (as described in Section 24 of these Policies and Procedures), no major changes to the IRB approval, and the Research Project budget or the amount of the external funding has been determined by the Facility Financial Analyst (as defined in Section 33.2) to be sufficient to cover the next year's expenses, then the Research Project will be reviewed at the Facility and H+H Central Office levels and renewed for a term of no greater than one (1) year based on the IRB expiration date. Upon H+H Central Office approval, a continuation approval letter will be sent to the Principal Investigator, Facility Research Administrators, and the Office of Research Administration.

12.2.3 New Application. If there have been Major Protocol Violations or major changes in operational feasibility or the scope of work has changed remarkably, the FRC and FRRC Chair will decide if a new application must be made and a complete review will take place via STAR.

12.2.4 Multi-Facility Approvals. Each Facility involved in a Research Project should request continuing approval individually.

SECTION 13. LAPSED STUDIES, SUSPENSIONS & TERMINATION OF RESEARCH PROJECT

13.1 Policy

In order to protect H+H's and its researchers' financial, contractual, and legal interests, H+H has the authority to approve the commencement, continuation, suspension or termination of any Research Project based on Human Subject safety concerns, or based on financial, contractual, or legal reasons. This authority is in addition to approval or re-approval granted through the H+H Approval process discussed above in Section 4 and Section 12.

Additionally, all Research Projects that have not received H+H continuing approval through STAR will automatically move to the lapsed state after the date of H+H approval expires.

Active and lapsed studies are subject to suspension or termination if deemed necessary by Facility, Corporate Administrators, Sponsors or IRBs.

Subject to law and the terms of the governing Research agreement, if applicable, H+H may suspend enrollment of all Human Subjects or terminate a Research Project as set forth below.

13.2 Procedure

13.2.1 *Termination or Suspension upon IRB Determination or Other Factors.* The Facility, corporate administrators, Sponsors or IRBs may suspend or terminate a Research Project if deemed necessary.

(a) H+H may suspend or terminate a Research Project in accordance with such determination by the applicable IRB. Upon receiving such determination in accordance with the applicable IRB authorization agreement and after so instructing the Principal Investigator, the FRC will suspend the project in STAR. The Principal Investigator must fulfill any actions required by the IRB when termination or suspension involves the withdrawal of current Human Subjects from the Research Project.

(b) Subject to law and the terms of the governing Research agreement, if applicable, H+H may suspend enrollment of all Human Subject or terminate a Research Project if H+H, in consultation with the IRB and Principal Investigator, has determined that there are Human Subject safety concerns, or based on financial or administrative reasons.

13.2.2 *Failure to Apply for Continuing Approval.* Principal Investigators must keep all IRB documents current in STAR. Failure to do so will result in the study moving to the lapsed state. Studies in the lapsed state should not continue study activities until H+H approval is renewed unless except when continuity of care must be considered as determined by the PI or treating physician.

13.2.3 Continuity of Care. Upon termination or suspension of a Research Project under this Section, the Principal Investigator shall provide a plan for the continuity of medical care for current Human Subjects withdrawn from such Research Project in accordance with OHRP guidance,⁸⁹ the Principal Investigator's professional ethical responsibilities, and as required by the IRB and applicable law.

SECTION 14. RESEARCH PROJECT CLOSURE

14.1 Policy

All Research Projects that are approved through STAR must be closed upon completion, or earlier if terminated or suspended prior to the Research Project's completion.

14.2 Procedure

14.2.1 Principal Investigators must submit a closure application of each Research Project in STAR. A closeout or termination letter from the IRB should be submitted as part of this closure. The Facility and H+H Central Office are responsible for reviewing the Principal Investigator's request and ensuring that the study is closed within STAR. Upon H+H Central Office approval, a closure notification will be sent to the Principal Investigator, Facility Research Administrators, and Office of Research Administration.

14.2.2 Principal Investigators should ensure that the study has been closed with the Grantor, Funder, or and that all research costs have been reconciled.

SECTION 15. AUDITING, ON-GOING MONITORING AND COMPLIANCE ACTIVITIES

15.1 Policy

H+H has an obligation under its FWA to take appropriate action with respect to any Research Project where the safety of Human Subjects is at issue. As such, H+H will conduct quality assurance activities and ensure that any of its contractors conduct their responsibilities with respect to Research in accordance with H+H's quality assurance requirements and obligations, to the extent applicable. Research Projects are eligible for monitoring and full audits by H+H after the first Human Subject is enrolled.

In instances where H+H has delegated the review of Research Protocols under its FWA to an outside IRB, H+H is responsible for conducting quality assurance activities to ensure that the IRB performs its review activities in a safe and effective manner.

15.2 Procedures

15.2.1 Monitoring. The Office of Research Administration may request the monitoring reports from Sponsors or the Principal Investigator, if applicable. If the Office of Research Administration has made a determination to conduct an independent investigation, the Office of Research Administration, in collaboration with the IRB that approved a Research Project,

may conduct on-going monitoring and/or audit each such Research Project on a periodic basis that is frequent enough to ensure compliance with all applicable laws and policies and procedures of H+H. Monitoring shall be conducted in accordance with the responsible IRB's policies and procedures. An audit will consist, at a minimum, of meeting with the Principal Investigator and reviewing Research Protocol documentation, to verify that the following Research documents are maintained:

- (a) Research Protocol, including all supporting documents (data abstraction forms, recruitment materials, advertisements, etc.) as approved by the IRB and H+H;
- (b) Informed Consent, assent, parental permission document(s), if applicable, and Research Authorization Form as approved by H+H and the IRB;
- (c) Current documentation of training regarding Research involving Human Subjects, CV and medical license, if applicable;
- (d) Approval letters from the IRB and from the Office of Research Administration to start the Research Project;
- (e) Letters approving continuing review and the final report;
- (f) Human Subject research source documentation and Human Subject medical record information;
- (g) Review of financial and time and effort compliance in accordance with H+H Operating Procedure 40-61: Time and Effort Reporting and Operating Procedure;
- (h) All correspondence between investigators, Office of Research Administration, Grantor/Sponsor and reviewing IRB(s); and
- (i) Any other documentation as determined by the IRB and H+H.

15.2.2 Audits.

(a) *Frequency and Scope.* The Office of Research Administration, in collaboration with the applicable IRB, will also perform audit activities at least every two years during ongoing Research Projects, which can include, but are not limited to:

- (i) Verification that Research documents and databases are sufficiently secured to maintain privacy and confidentiality of data as described in the Research Protocol;
- (ii) Verification that the Principal Investigator is appropriately tracking selected options regarding the future use of specimens, etc., as described in the Informed Consent documentation and the approved Research Protocol;

(iii) Quality assurance activities to monitor the activities of the IRB to confirm that the IRB is properly protecting the safety and interests of Human Research Subjects.

(b) *External Audit Requests.*

(i) Audit requests from external regulatory agencies should be directed to the Office of Research Administration. The Office of Research Administration will work with the Principal Investigator and Facility as necessary to respond to the audit request. The Office of Corporate Compliance and the Office of Legal Affairs shall be promptly informed of any external audits conducted by regulatory bodies.

(ii) All inquiries from Federal, State and local law enforcement agencies must be promptly directed to the Office of Inspector General in accordance with H+H Operating Procedure 30-1.

(c) IRB Audits

(i) IRBs are permitted to conduct independent audits of Research Projects. The results of these audits should be directly communicated to the Office of Research Administration.

15.2.3 Compliance Activities.

(a) *Communication with Office of Corporate Compliance.* The results of all audits under Section 15.2.2 will be shared with the Office of Corporate Compliance.

(b) *Participation in Research Compliance.* The RA Director and chair of the Research Council will serve on a research compliance committee as designated and chaired by the Chief Corporate Compliance Officer. Such committee will meet as often as deemed necessary or otherwise stipulated under H+H Operating Procedure 50-1 (Corporate Compliance Program) or any other applicable H+H policy or procedure.

(c) *Independent Audits and Monitoring.* H+H reserves the right to retain outside consultants or independent auditors to assist with the monitoring or audit of Research compliance. If an outside consultant or independent auditor is utilized to review H+H Research activities, any findings from such review must be reported to the Office of Corporate Compliance.

(d) *Office of Corporate Compliance.* The Office of Corporate Compliance may conduct audits as it deems necessary to maintain an effective corporate compliance program as set forth under H+H Operating Procedure 50-1 (Corporate Compliance Program).

15.2.4 The CMO, in conjunction with the Office of Research Administration shall perform quality assurance reviews of H+H's overall Human Subjects protection program as outlined in OHRP's QA Self-Assessment Tool, attached as **Exhibit 11**, at least once every two (2) years.

PART IV

INVESTIGATIONAL DRUGS, DEVICES, AND BIOLOGICAL MATERIALS

SECTION 16. USE OF INVESTIGATIONAL NEW DRUGS AND DEVICES

16.1 Investigational New Drugs

16.1.1 Policy

Subject to certain exemptions, FDA regulations require that Research involving the use of an Investigational Drug be conducted under an IND. The FDA's primary objectives in reviewing INDs is to protect the rights and safety of Human Subjects and to help ensure that the quality of the clinical trial is adequate to evaluate the Investigational Drug's effectiveness and safety.⁹⁰ Principal Investigators who conduct Research involving Investigational Drugs must know and comply with all relevant FDA regulations governing the use of Investigational Drugs. This Section outlines procedures for determining if Research is eligible for an IND exemption.

16.1.2 Definitions

"Biological Product" means a biological or related product, regulated by the FDA, including blood, vaccines, allergenics, tissues, and cellular and gene therapies.

"IND" means an Investigational New Drug application submitted to the FDA in accordance with 21 C.F.R. § 312.20.

"Investigational Drug" means a new drug or biologic that has not yet been approved by the FDA or an approved drug or biologic that has not yet been approved for a new use and is in the process of being tested for safety and effectiveness.

"Sponsor-Investigator" means an individual who both initiates and actually conducts, along or with others, a clinical investigation and under whose immediate direction the Investigational Drug or Investigational Device is administered, dispensed, or used.

16.1.3 Procedures

(a) Research may be eligible for an IND exemption if it meets one of the following exceptions:⁹¹

(i) The Research involves a drug that is lawfully marketed in the United States and all of the following apply:

(1) The Research is not intended to be reported to FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;

(2) If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;

(3) The Research does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;

(4) The Research is conducted in compliance with the requirements for IRB review and Informed Consent as set forth in 21 C.F.R. Parts 56 and 50, respectively;

(5) The Research is conducted in compliance with the requirements of 21 C.F.R. § 312.7.

(ii) The Research is for an in vitro diagnostic Biological Product involving (a) blood grouping serum; (b) reagent blood cells; and (c) anti-human globulin and either of the following apply:

(1) The Research is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and

(2) The Biological Product is shipped in compliance with 21 C.F.R. § 312.160.

(iii) The Research involves the use of a placebo and does not otherwise require submission of an IND.

(b) The Principal Investigator conducting Research under an IND will be responsible for ensuring:⁹²

(i) Research conducted under an IND is conducted according to the signed investigator statement, the investigational plan, and applicable regulations;

(ii) The rights, safety, and welfare of Human Subjects under the Principal Investigator's care are protected;

(iii) Control of the Investigational Drug under investigation;

(iv) Informed Consent is obtained of each Human Subject to whom the drug is administered as required by 21 C.F.R. Part 312, Subpart B;

(v) The Investigational Drug is administered only to Human Subjects under the Principal Investigator's personal supervision or under the supervision of a Sub-investigator responsible to the Principal Investigator;

(vi) The Investigational Drug is supplied only to individuals authorized to receive it;

(vii) Adequate records of the disposition of the Investigational Drug are maintained, including dates, quantity, and use by Human Subjects;

(viii) If the Research is terminated, suspended, discontinued, or completed, unused supplies of the Investigational Drug are returned to the Sponsor, or otherwise disposed of as instructed by the Sponsor;

(ix) Adequate and accurate case histories are prepared and maintained, that record all observations and other data pertinent to the Research on each Human Subject administered the Investigational Drug or employed as a control in the Research. Case histories include the case report forms and supporting data including signed and dated consent forms and medical records. The case history for each individual shall document that Informed Consent was obtained prior to participation in the Research;

(x) Records are retained for a period of two (2) years following the date a marketing application is approved for the Investigational Drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until two (2) years after the investigation is discontinued and the FDA is notified;

(xi) All progress reports, safety reports, and financial disclosures are furnished to the Sponsor and to the IRB;

(xii) An IRB is responsible for the initial and continuing review and approval of the Research, and all changes in the Research that occur without IRB approval are promptly reported to the IRB, except where necessary to eliminate apparent immediate hazards to Human Subjects;

(xiii) Authorized individuals are permitted to have access to, and to copy and verify any relevant records.

16.2 Investigational Device Exemptions

An IDE allows an Investigational Device to be used in a clinical study in order to collect safety and effectiveness data. Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices. Per FDA regulations, all clinical evaluations, unless exempt, must have an approved IDE before the study is initiated.⁹³

16.2.1 Policy

H+H requires that Research involving Investigational Devices be conducted in accordance with all applicable Federal regulations.⁹⁴

16.2.2 Definitions

“**IDE**” refers to the regulations under 21 C.F.R. § 812. An approved IDE means that the IRB (and the FDA for SR Devices) has approved the Sponsor’s study application and all the requirements under 21 C.F.R. § 812 are met.

“**Investigational Device**” means a device, including a transitional device that is the object of a clinical investigation or Research involving one or more Human Subjects to determine the safety and/or effectiveness of a device.

“**Non-Significant Risk (NSR) Device**” means a device that is not a Significant Risk Device, as defined below.

“**Significant Risk (SR) Device**” means a device that presents a potential for serious risk to the health, safety, or welfare of a Human Subject and is: (1) intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating, or treating a disease, or otherwise prevents impairment of human health, or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a Human Subject.

16.2.3 Procedures

(a) When Research is being conducted to determine the safety and effectiveness of a device, a determination must be made as to whether the device qualifies for an exemption⁹⁵ and, if not, whether the device is an SR Device for which an IDE is required or a NSR Device subject to abbreviated requirements.⁹⁶ The initial determination of whether or not a device is a SR Device or a NSR Device is made by the Sponsor and presented to the IRB for review.⁹⁷ If the Sponsor has not already done so, the Principal Investigator must make this determination and present it to the IRB to determine whether the assessment is appropriate. If a NSR Device qualifies as “minimal risk” under the FDA regulations, the IRB may choose to review the study under expedited procedures. The IRB’s risk determination is made based on both the nature of the device and the proposed use of the device in the study. If the IRB determines that a device qualifies as an SR Device, it is required to notify the Principal Investigator and, where appropriate, the Sponsor of the study.⁹⁸

(b) The Principal Investigator of a device study will be responsible for ensuring:⁹⁹

(i) The IRB is provided with the Sponsor’s risk assessment and, in the case of an NSR Device, the Sponsor’s rationale for its determination;

(ii) Research is conducted according to the signed agreement, the investigational plan, and applicable FDA regulations, and any conditions or approval imposed by the IRB or FDA;

(iii) The rights, safety, and welfare of Human Subjects under the Principal Investigator's care are protected, and for the control of devices under investigation;

(iv) Informed Consent is obtained in accordance with 21 C.F.R. Part 50 and all other regulatory requirements.¹⁰⁰ A Principal Investigator may determine whether potential Human Subjects would be interested in participating in an investigation, but may not request the written Informed Consent of any Human Subject, nor allow any Human Subject to participate, before obtaining IRB and FDA approval;

(v) The Investigational Device is used only with Human Subjects under the Principal Investigator's supervision, and is not supplied to any person not authorized to receive it;

(vi) All required financial disclosures are provided to the Sponsor and the IRB;

(vii) Upon completion or termination of an investigation, or at the Sponsor's request, any remaining supply of the Investigational Device is returned to the Sponsor or otherwise disposed of as the Sponsor directs.

16.3 Humanitarian Use Devices

16.3.1 Policy

(a) A Humanitarian Use Device ("HUD") is a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year.

(b) H+H requires that Research involving a HUD be conducted in accordance with all applicable Federal regulations.¹⁰¹

16.3.2 Procedure

(a) A HUD may be administered only if such use has been approved by the IRB. In an emergency situation where prior 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 such an emergency situation, the Principal Investigator shall, within five (5) days after use of the HUD, provide written notification to the IRB of such use, which must include identification of the patient involved, the date on which the HUD was used, and the reason for the use.¹⁰²

(b) All HUD uses must be entered into the STAR system with copy of the IRB approval within thirty (30) calendar days of obtaining IRB approval.

16.3.3 Principal Investigator as Sponsor. When a Principal Investigator holds an IND or an IDE as a Sponsor-Investigator, the Principal Investigation is required to comply with all FDA requirements for Sponsors in addition to those for Principal Investigators.

SECTION 17. EXPANDED ACCESS AND EMERGENCY USE OF INVESTIGATIONAL DRUGS AND DEVICES

Expanded access, also called “compassionate use,” is the use of a Test Article (as defined below) outside of a clinical trial. Expanded access may be available for patients with a Serious Disease or Condition or an Immediately Life-threatening Disease or Condition¹⁰³ who lack therapeutic alternatives.¹⁰⁴

17.1 Policy

H+H recognizes the importance of providing patients with expanded access, including expanded access for emergency use, when a patient is experiencing a Serious Disease or Condition or an Immediately Life-Threatening Disease or Condition and has no comparable or satisfactory alternative treatment options. If a Principal Investigator desires to use Test Article for Expanded access, it must first notify the IRB and then the Office of Research Administration. Principal Investigators must understand and abide by all FDA requirements regarding expanded access use of Test Articles, particularly those specifically applicable to Principal Investigators as set forth in 21 C.F.R. Part 312 Subsection D, and 21 C.F.R. Part 812 Subsection E, respectively. For more information on these requirements, Principal Investigators should review the following FDA guidance documents:

- *Expanded Access to Investigational Drugs for Treatment Use – Guidance for Industry*, available at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM351261.pdf>, and
- *Expanded Access for Medical Devices*, available at <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm#compassionate>.

17.2 Definitions

“Immediately Life Threatening Disease or Condition” means a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

“Serious Disease or Condition” means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgement, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one.

“**Test Article**” means an Investigational Drug or an Investigational Device.

17.3 Procedure

17.3.1 Expanded Access Use of an Investigational Drug

(a) Any agreements required for the expanded access use of an Investigational Drug must be reviewed and approved by the Office of Research Administration and the Office of Legal Affairs prior to signature.

(b) Before taking any other steps, the Principal Investigator must notify the Office of Research Administration of his or her desire to use an Investigational Drug for expanded access purposes. The notification should be in writing and should identify the Investigational Drug to be used and the Facility where the use will take place.

(c) When a Principal Investigator would like to obtain an Investigational Drug for expanded access use, the Principal Investigator should first ensure that the Investigational Drug can be obtained. If so, the Principal Investigator should obtain a Letter of Authorization (“LOA”) from the entity that is the Sponsor of the IND (e.g. commercial sponsor or drug manufacturer) being referenced. If an LOA is not available, the Principal Investigator should contact the relevant review division at the FDA to determine what information is necessary to support the expanded access submission.¹⁰⁵

(d) An expanded access submission to the FDA must include all of the information required by 21 C.F.R. § 312.305(b) and 21 C.F.R. § 312.310(b). Additionally, the Principal Investigator must determine that the probable risk to the Human Subject for the Investigational Drug is not greater than the probable risk from the disease or condition and the Human Subject cannot obtain the Investigational Drug under another IND or protocol.¹⁰⁶ Treatment may begin thirty (30) days after FDA receives the submission, or upon earlier notification from the FDA that the treatment use described in the protocol may or may not begin.¹⁰⁷

(e) A Principal Investigator treating a patient with an Investigational Drug under expanded access is responsible for obtaining IRB review and approval consistent with the requirements of 21 C.F.R. Part 56 before treatment with the Investigational Drug may begin, regardless of whether the protocol is submitted in a new IND or to an existing IND.¹⁰⁸ The Principal Investigator should submit a copy of all material prepared for the FDA approval to the IRB.

(f) A Principal Investigator treating a patient with an Investigational Drug under expanded access is responsible for ensuring that the Informed Consent requirements of 21 C.F.R. Part 50 are met and for maintaining accurate case histories and drug disposition records and maintaining records in compliance with the requirements of 21 C.F.R. § 312.62.¹⁰⁹

17.3.2 Expanded Access Use of an Investigational Device

(a) Any agreements required for the expanded access use of an Investigational Device must be reviewed and approved by the Office of Research Administration and the Office of Legal Affairs prior to signature.

(b) Before taking any other steps, the Principal Investigator must notify the Office of Research Administration of his or her desire to use an Investigational Device for expanded access purposes. The notification should be in writing and should identify the Investigational Device to be used and the Facility where the use will take place.

(c) If a Principal Investigator would like to obtain an Investigational Device for an individual patient, the device manufacturer must first agree to provide the Investigational Device for expanded access purposes.¹¹⁰ If the device manufacturer agrees to provide the device under expanded access, the Principal Investigator should request the manufacturer to prepare a supplement to the IDE for submission to the FDA for review and approval.

(d) If there is an IDE for the Investigational Device, the IDE Sponsor (who may be the device manufacturer or a physician who has submitted the IDE to conduct the clinical study for the device) should submit an IDE supplement requesting approval for expanded access use under 21 C.F.R. § 812.35(a) in order to treat the patient. The IDE supplement should contain the following information:

(i) A description of the patient's condition and the circumstances necessitating treatment;

(ii) A discussion of why alternative therapies are unsatisfactory and why the probable risk of using the Investigational Device is no greater than the probable risk from the disease or condition;

(iii) An identification of any deviations in the approved clinical protocol that may be needed in order to treat the patient;

(iv) The patient protection measures that will be followed, including:

(1) A draft of the Informed Consent form;

(2) Clearance from H+H, including from the Office of Research Administration;

(3) Concurrence from the IRB;

(4) Documentation of an independent assessment from an uninvolved physician; and

(5) Authorization from the device manufacturer for the use of the device.¹¹¹

(e) The Principal Investigator may not begin treatment until thirty (30) days after the FDA receives the treatment IDE submission, unless the FDA provides earlier notification that the treatment use may or may not begin.¹¹²

(f) Once FDA approves the use of the Investigational Device, the Principal Investigator must seek concurrence from the IRB to proceed with the use of the Investigational Device. The Principal Investigator should submit a copy of all information prepared for the FDA's approval to the IRB.

17.3.3 Emergency Use of Test Article. Under certain circumstances, H+H permits emergency use of an unapproved Test Article intended to benefit a single patient who is not enrolled in or eligible for a Research Project if the patient is experiencing a Serious Disease or Condition or a Life Threatening Disease or Condition that requires immediate treatment and no generally acceptable alternative for treating the patient is available. Emergency uses of Test Articles are exempt from the requirement to obtain prior IRB review and approval, provided that the use is reported to the IRB within five (5) working days after initiation of the emergency use.¹¹³

(a) General Requirements for the Emergency Use of Test Articles

(i) Any agreements required for emergency use must be reviewed and approved by the Office of Research Administration and the Office of Legal Affairs prior to signature.

(ii) Before taking any other steps, a Principal Investigator must notify the Office of Research Administration of his or her desire to use an Test Article for emergency purposes. The notification may be in writing or by phone and should identify the Test Article to be used and the Facility where the use will take place.

(iii) *Prior to the Emergency Use*

(1) Principal Investigators are encouraged to obtain consultation from an IRB chair prior to the emergency use of a Test Article, whenever possible.

(2) Principal Investigators should attempt to identify any protocols already approved by the applicable IRB using the same Test Article for which the recipient might qualify.

(3) Principal Investigators are responsible for confirming that there has not been a prior emergency use of the Test Article.

(4) Principal Investigators are responsible for obtaining approval of a second use of a Test Article that has been used previously in a prior emergency use from the Facility's medical director.

(5) Principal Investigators are responsible for obtaining an independent assessment and approval for the emergency use of a Test Article and, if applicable, for the exception to the Informed Consent requirement from the Facility's medical director/designee. The Facility's medical director or a designee should provide the assessment and approval if the Facility's medical director is involved in the recipient's care. The Facility's medical director (or designee) shall document his or her determinations and sign and date where required.

(6) Principal Investigators are responsible for complying with any H+H policies regarding receipt, dispensing, use and/or control of Test Articles.

(7) Principal Investigators are required to submit a report to the IRB in accordance with the time frame and manner specified in the applicable IRB policies. Principal Investigators upload a copy of the report to the STAR system in a timely manner.

(8) Principal Investigators are responsible for ensuring that the recipient of the emergency Test Article is not included in a systematic investigation designed to develop or contribute to generalizable knowledge.

a. This above provision does not limit the provision of outcomes or safety information as required by the FDA.

b. The above provision does not preclude the retrospective use of data (under appropriate IRB review and approval for such a Research Project).

c. The above provision does not preclude the use of information in publication or presentation of a case history. When publishing or presenting more than one case, please contact the H+H Office of Legal Affairs to ascertain whether this constitutes Research requiring IRB and H+H review and approval.

(iv) *After the Emergency Use*

(1) If immediate use of the Test Article is, in the Principal Investigator's opinion, required to preserve the life of the Recipient, and time is not sufficient to obtain independent certification of the criteria listed above in advance of using the Test Article, the determinations of the Principal Investigator shall, within five (5) business days after the emergency use, report the emergency

use to the IRB and have the emergency use be reviewed and evaluated by the Facility's medical director.

(2) Subsequent to the emergency use, the Principal Investigator and the Facility's medical director are encouraged to evaluate the potential for future use of the Test Article at H+H, and, if necessary, work with the department chair and Office of Research Administration to initiate efforts to obtain approval from H+H, the appropriate IRB, and regulatory clearance from the FDA to allow for the broadest possible future use of the drug.

(b) Informed Consent for Emergency Use of a Test Article. Prior to use, the Principal Investigator must either obtain the Informed Consent of the prospective recipient or a legally authorized representative in accordance with the FDA requirements outlined in 21 C.F.R. § 50.25, or determine that the emergency use meets the criteria for an exception to the requirement for Informed Consent, as detailed below.¹¹⁴

(1) FDA regulations¹¹⁵ provide for an exception from general requirements for Informed Consent if the Principal Investigator and a physician not otherwise involved in the emergency use, submit a written certification to the IRB within five working days after the use of the Test Article that all of the following criteria are met:

(2) The prospective recipient is confronted by a life-threatening situation necessitating the use of the Test Article.

(3) Informed Consent cannot be obtained from the recipient because of an inability to communicate with, or obtain legally effective consent from, the recipient.

(4) Time is not sufficient to obtain consent from the recipient's legal representative.

(5) There is no available alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the recipient.

(c) Specific Requirements for the Emergency Use of Investigational Drugs

(i) *FDA Authorization.* Prior FDA authorization is required for emergency use of Investigational Drugs. The Principal Investigator is responsible for obtaining this authorization in accordance with applicable laws and regulations. The request for emergency use is usually communicated to the FDA by telephone or other means of rapid communication. Treatment with the Investigational Drug may start

immediately upon FDA authorization, and the Principal Investigator must agree to submit a written submission to the FDA within fifteen (15) working days of the initial FDA authorization.¹¹⁶ More information regarding how to request FDA authorization for emergency use of investigational drugs can be found on the FDA website at *Emergency Investigational New Drug (EIND) Applications for Antiviral Products*, available at <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm090039.htm>.

(ii) *Initial Use.* FDA permits one emergency use of an Investigational Drug per institution without prospective IRB review. FDA requires that any subsequent use of the Investigational Drug at the institution have prospective IRB review and approval.

(iii) Emergency use of an Investigational Drug also requires an exemption from the approved use of the Investigational Drug. This may be accomplished in one of three ways:

(1) The Principal Investigator identifies an existing Research Protocol for the same Investigational Drug that is already approved by the IRB and for which the Recipient may be enrolled and is able to provide consent according to the requirements of the protocol and its IRB approval. In this case, the emergency use procedure is not needed. If an enrollment exception is needed in order to enroll the Recipient, the Principal Investigator should consult the Sponsor.

(2) The Principal Investigator should communicate with the holder of an IND for the product (such as the manufacturer) to ascertain whether the emergency use may occur under an existing IND and the IND holder is willing to provide the Test Article.

(3) If the use may not occur under an existing IND, but the IND holder is willing to provide the Test Article, the Principal Investigator must obtain an IND from the FDA. If the situation does not allow time for submission of an IND, the FDA may issue an authorization of shipment in advance of an IND.

(iv) *Second Use.* FDA guidance acknowledges that it would be inappropriate to deny an Investigational Drug to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the second use. In cases in which an IRB does not have sufficient time to convene, a determination regarding acceptability of the second use of an Investigational Drug in an emergency situation must be made by the Facility's Medical Director or his/her designee, as discussed in Section 18.2.3(e).

(d) Specific Requirements for the Emergency Use of Investigational Devices. In the event that the Principal Investigator determines that an emergency use of an Investigational Device is needed, the Principal Investigator must contact the IRB and should consult with the Office of Research Administration for guidance with respect to such emergency use.

(e) Second Use of a Test Article.

(i) In cases where a Test Article has previously been used in an emergency at H+H, but the IRB has not had sufficient time to convene a meeting to review the issue, the Facility's medical director (or a designee if the Facility's medical director is involved in the care of the recipient) must make a prospective determination regarding the acceptability of a second use of the Test Article in an emergency situation using the following criteria:

(1) The Facility's medical director or designee must determine that although the Test Article has been used at H+H in a previous emergency, there is insufficient time to obtain IRB review and approval for the second emergency use.

(2) The determination must also include justification for the additional use.

(3) The determination must be made prior to emergency use.

(ii) The Principal Investigator or the Facility's medical director or designee must notify the Office of Research Administration of the second use of a Test Article for emergency purposes as soon as reasonably practicable under the circumstances, but in no event more than twenty-four (24) hours after the second use of the Test Article.

(iii) A written statement of the determinations regarding the second use, signed and dated by the Facility's medical director or designee, must accompany the Principal Investigator's post-use report to the IRB.

17.3.4 STAR Record. A record of any use of a Test Article must be recorded in the STAR system, along with a copy of the IRB approval, within thirty (30) calendar days of receiving such approval. For emergency use of a Test Article, the record must be uploaded within thirty (30) days after notifying the IRB of such emergency use.

SECTION 18. STORAGE, HANDLING & DISPENSING INVESTIGATIONAL DRUGS & BIOLOGICS

18.1 Policy

All Investigational Drugs, agents, or Biologics in use at an H+H Facility must be stored, handled, and dispensed in accordance with FDA, Federal and New York State Boards of Pharmacy regulations and guidance, and H+H policies and procedures. Controlled substances in use at H+H Facilities are also subject to particular licensing requirements under Federal and New York State laws.

18.2 Definitions

For purposes of this Section 18, the following definitions shall apply.

“**Biologic**” means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.¹¹⁷

“**Investigational Brochure**” or “**IB**” refers to a comprehensive document summarizing all known information about an investigational agent.¹¹⁸ This includes all basic chemistry, pharmacology, toxicology, pre-clinical and clinical data to date, and summaries of non-clinical studies, clinical trials and adverse experiences with the investigational agent.

“**Study Monitor**” means the individual appointed by the Sponsor/Grantor, as applicable, responsible for assuring the protection of Human Subjects, the accuracy and completeness of reported trial data, and the compliance of the trial with the protocol, good clinical practices and applicable regulations.¹¹⁹

18.3 Procedures

18.3.1 Roles and Responsibilities.

(a) *Sponsor/Grantor.* All Investigational Drugs and supplies required by a Research Protocol being studied under an IND must be provided by the Sponsor/Grantor, as applicable.¹²⁰

(b) When necessary, an external Pharmacy can be utilized if the Facility Pharmacy is unable to adhere to the requirements for storing, dispensing and handling of the Investigational Drug. If an external Pharmacy is required, the Principal Investigator should contact the H+H Office of Research Administration immediately.

(c) *Facility Pharmacy/Pharmacist.*¹²¹ The Facility Pharmacist is responsible for the receipt, storage, security, labeling, dispensing, and disposition

of all Investigational Drugs and supplies used in clinical investigations. The Facility Pharmacist has the following responsibilities:

(i) Ensuring that the Facility Pharmacy has access to all of the following:

- (1) An IRB approval letter;
- (2) A copy of the approved Research Protocol;
- (3) An Investigational Brochure, when appropriate;
- (4) Any Sponsor/Grantor -provided documents relating to the storage, preparation, dispensing, and accountability of the investigation products;
- (5) Protocol revisions, amendments, and updates after IRB approval and after the IRB approved the amendment;
- (6) Updates and changes to authorized prescribers after IRB approval;
- (7) Documentation of IRB continuing review and approval;
- (8) Notice if clinical investigation is suspended or terminated by the IRB, FDA, or other oversight group (e.g., the Sponsor/Grantor);
- (9) Notice of when the study is closed; and
- (10) The Investigational Drug information on each patient receiving an Investigational Drug.

(ii) Ensuring that, prior to commencing Research, there is adequate pharmacy staffing and resources to safely conduct Research Projects involving Investigational Drugs in compliance with all rules and regulations,¹²² taking into consideration the pharmacy staff's time in all phases of the Research Project from protocol review and study initiation to drug and supply returns and study closure, as well as physical space and equipment.

(iii) Ensuring that all Research pharmacy staff having direct responsibilities for the management, dispensing and oversight of Investigational Drugs and Biologics are appropriately trained with respect to Human Subject protections as required by the applicable IRB.¹²³

(iv) Ensuring the receipt, maintenance, review, and compliance with Research Protocol documents and approvals.

(v) Verifying that the Research Project involving the Investigational Drug has received initial approval and funding, prior to ordering, receipt, storage, or dispensing of Investigational Drugs.

(vi) Maintaining documentation of approved clinical investigations using Investigational Drugs or supplies and commercial drugs, including Research Protocols, completed Informed Consent forms, and a real time Investigational Drug Accountability Log (see **Exhibit 12**) described in Section 18.3.3.¹²⁴

(vii) Retaining the Research Protocol documents and Investigational Drug Accountability Log maintained by the Facility Pharmacy according to H+H policy and procedures with respect to Research records, FDA regulations or Sponsor/Grantor requirements, whichever time period is longest.¹²⁵

(viii) Obtaining approval from the Sponsor/Grantor prior to destroying records.

(ix) Obtaining a signed Informed Consent form prior to dispensing an Investigational Drug.

(d) Making available for inspection by the Study Monitor a patient specific source chart.

18.3.2 Investigational Drug and Supply Management.

All Investigational Drug and supply management must remain under the direction of the Facility Pharmacy.¹²⁶

18.3.3 Receipt of Investigational Drugs.

(a) Regardless of the source, all investigational and Sponsor/Grantor supplied drugs must be delivered to the Facility Pharmacy for receipt, storage, security, labeling, distribution, dispensing, and disposition.

(b) Investigational Drugs may be obtained from other Facilities or Principal Investigators only where evidence of an approved Letter of Understanding (LOU) is provided, and in adherence to Research Protocol procedures and FDA requirements. Where an LOU has not yet been executed, the LOU template in **Exhibit 13** can be used in negotiations. An LOU can exist between a Facility and an H+H Affiliate, provided that investigators at the Facility and H+H Affiliate are both participating in the Research Project utilizing the Investigational Drug.¹²⁷

(c) Detailed information as to how drugs are to be dispensed and accounted for must be clearly stated in the Investigational Drug Accountability Log (see **Exhibit 12**).

18.3.4 Storage and Accountability. The Facility shall ensure that:

(a) Investigational Drugs and supplies must be securely stored in the pharmacy; they must be kept separate from all non-Investigational Drugs and supplies; and they must be clearly identified as to which study they are assigned.

NOTE: Although New York regulations require that all drugs and biologics be stored in a locked storage area,¹²⁸ storage of Investigational Drugs or Biologics does not require segregation to a separate locked area within a pharmacy, unless the medication has specific storage requirements.

(b) Investigational Drugs must be stored according to the requirements of the Sponsor/Grantor (room temperature, refrigerated, in freezer, etc.) and routinely monitored.

(c) The Investigational Drug Accountability Log (**Exhibit 12**) or an accountability record, authorized by H+H and the Grantor/Sponsor must be completed in real time and maintained by the Facility Pharmacy.

(d) All electronic drug accountability records that are created, modified, maintained, archived, retrieved, or transmitted, under any records requirements set forth by the FDA, including the Investigational Drug Accountability Log in **Exhibit 12**, must be compliant with the FDA's regulations governing electronic records and electronic signatures.¹²⁹

(e) Clinical investigations involving controlled substances must meet the same storage and accountability requirements as outlined for routine patient care and in accordance with applicable laws, regulations, and H+H policies. In addition to the storage requirements for non-controlled study medications, the following requirements and detailed information must be kept for controlled substance study drugs:

(i) Controlled substance review and inventory requirements as specified in H+H policies and procedures;

(ii) All controlled substance dispensing;

(iii) Controlled substances returned (including drugs drawn up, but not used);

(iv) All controlled substance record reconciliations;

(v) Controlled substances wasted; and

(vi) Controlled substance use, categorized by Principal Investigator and/or prescriber.

(f) A final entry is made when drug therapy for the entire Research Project has ended. This entry documents the date of termination of the use of the Investigational Drug, the quantity remaining, the action taken to dispose of the

balance on hand, and the agent or individual responsible for drug destruction or return.

(g) Investigational Drug or supply returns and destruction need to follow the requirements as outlined in the Research Protocol.

18.3.5 Dispensing.

(a) Investigational Drugs and supplies can only be dispensed directly to Human Subjects, the legally-authorized representative, or authorized-Research Project personnel.

(b) Investigational Drugs and supplies may be dispensed only after a provider, who is authorized to prescribe the drug, has submitted a proper written or electronic order.

(c) Investigational Drug prescriptions may be entered into the computerized patient record system by an investigational drug pharmacist at the Facility Pharmacy.

(d) The initial order or prescription for each new Human Subject on an investigational protocol must be accompanied by a signed Informed Consent and made available to the Facility Pharmacy.

(e) The Investigational Drugs and/or supplies must be prepared, labeled, and dispensed according to the Research Protocol requirements, H+H policies and procedures, and applicable law and regulations.

(f) In addition to the generally-required prescription label information and appropriate auxiliary caution or warning labels, all Investigational Drug labels must include the following legend:

**“CAUTION – NEW DRUG: LIMITED BY FEDERAL
LAW TO INVESTIGATIONAL USE.”¹³⁰**

(g) If compounding or admixing of the Investigational Drug is required by the Research Protocol, applicable United States Pharmacopoeial Standards¹³¹ and Good Clinical Practices must be followed.

(h) If a Sponsor or Grantor has additional dispensing requirements, these must be followed.

18.3.6 Drug and Supply Returns.

(a) In accordance with Federal regulations, Sponsors/Grantors generally require the Human Subject to return unused clinical investigation drugs and empty containers.¹³²

(b) Investigational Drugs and supplies returned by Human Subjects may not be re-dispensed.¹³³

(c) Investigational Drugs and containers returned by Human Subjects are to be stored separately from study supplies that have not been dispensed.

(d) Returned supplies are to be handled per the protocol's defined requirements.

SECTION 19. MATERIAL TRANSFER AGREEMENTS

19.1 Policy

H+H encourages researchers to exchange research materials with other scientists in academia, non-profit institutions, or those in industry who will use materials for Research purposes. In order to protect H+H and researchers from liability relating to the transfer and subsequent use and handling of the material, as well as to ensure H+H's and researchers' publication and intellectual property rights in the material, Principal Investigators must work with the Office of Research Administration and Office of Legal Affairs to enter into an appropriate Material Transfer Agreement ("MTA") with the third party prior to sending or receiving any research materials. Please see **Exhibit 14** for an example of H+H's MTA template.

19.2 Procedure

19.2.1 Sending Material:

(a) To send materials outside of H+H, the Principal Investigator must email the FRC, who will then notify the Office of Research Administration, the following information if not already included in the Research Protocol:

- (i) Name of the person to whom the material will be sent;
- (ii) The recipient's institution; and
- (iii) The name of the material.

(b) The Office of Research Administration will forward the appropriate documents to the Office of Legal Affairs for review and approval. Upon approval from the Office of Legal Affairs, the Office of Research Administration will forward the documents to the receiving party and notify the Principal Investigator when signatures have been obtained, thus allowing the Principal Investigator to send the materials.

19.2.2 Receiving Material. When seeking to acquire material from outside of H+H, if not already included in the Research Protocol, the Principal Investigator must forward all documents received from the provider of the materials to FRC, who will then notify the Office of Research Administration. The Office of Research Administration will consult with and obtain final

approval from the Office of Legal Affairs of the documents to protect the Principal Investigator's publication and other intellectual property rights, and to comply with H+H policies. The Office of Research Administration will keep the Principal Investigator informed throughout the negotiation process, and will provide the Principal Investigator with a fully executed copy of the MTA.

SECTION 20. USE OF TRANSFERRED BIOLOGICAL MATERIALS

20.1 Policy.

All Research conducted outside of a Research Protocol using Biological Materials shall be conducted in accordance with the applicable MTA (see Section 19, Material Transfer Agreements), Informed Consent and all applicable State and Federal laws regarding such Research. The Principal Investigator may collect, use, store, and disclose any specimens and/or tissue received only in accordance with the approved applicable Research Protocol and Informed Consent form, and in any event will not collect, use, store, or disclose any individually identifiable health information attached to or contained within the specimens and/or tissue in any manner that would violate any applicable law or regulation.

20.2 Definitions

For purposes of this Section 20, the following definitions shall apply.

“Biological Materials” means biological material of human origin including without limitation, tissues, blood, plasma, urine, spinal fluid or other fluids.

20.3 Procedures

As applicable, the Facility shall clearly mark and identify any and all Biological Materials transferred to an Affiliate, Grantor or Sponsor. As applicable, the Facility will enter into a materials transfer agreement with the Affiliate, Sponsor or Grantor, the specific form to be negotiated in good faith between the parties and in accordance with Section 19 of these Policies and Procedures (Material Transfer Agreements). No Facility shall transfer, deliver or otherwise release such Biological Materials to a third party (other than couriers and delivery service providers in the ordinary course of performing the Research) without the express prior written consent of H+H's Office of Legal Affairs.

SECTION 21. GUIDELINES FOR USE AND DISCLOSURE OF GENETIC INFORMATION

21.1 Policy

In addition to the Informed Consent required to be obtained from a Human Subject pursuant to the Common Rule and a Research Authorization Form, H+H requires that a consent conforming to the requirements of applicable law and this Section be obtained if Genetic Tests are to be conducted on any Biological Sample either as part of a Research Protocol in which the Human Subject is enrolled or is to be conducted on a stored Biological Sample as part of general research. Such Informed Consent may be obtained using the model Informed Consent for Research Involving

Genetic Testing, attached at Exhibit 15, or by incorporating the elements of that consent into the applicable Research Informed Consent, provided that the Research Informed Consent requires a separate signature that authorizes the performance of Genetic Testing and the use of Biological Samples for research purposes. To the extent a Research Project is reviewed by the IRB of an Affiliate, H+H will collaborate with that IRB to ensure the consent and corresponding genetic testing conforms to H+H's requirements.

Moreover, genetic information must also be kept confidential and be disclosed only as described in Sections 22.3.6 and 22.3.7. With respect to predispositional genetic testing, disclosure to any party must be specifically provided for in the Informed Consent. For any Research involving genetic testing or the use of genomic data, Principal Investigators must consult and comply with the Clinical Laboratory Standards of Practice for genetic testing set forth by the NYSDOH Wadsworth Center and the NIH Genomic Data Sharing Policy.

21.2 Policy

For purposes of this Section 21, the following definitions shall apply.

“Biological Sample” means any material part of the human body or of discharge there from known to contain DNA, including but not limited to tissue specimen, blood, or urine.

“Genetic Predisposition” means the presence of a variation in the composition of the genes of an individual or an individual's family member which is scientifically or medically identifiable and which is determined to be associated with an increased statistical risk of being expressed as either a physical or mental disease or disability in the individual or having offspring with a genetically influenced disease, but which has not resulted in any symptoms of such disease or disorder.

“Genetic Test” means 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.

“Genetic Testing Information” means that information described in Section 21.3.7(a).

21.3 Procedures

21.3.1 Conducting Genetic Testing as Part of Research.

(a) *General.* Before conducting Genetic Testing on a Biological Sample for Research, the Research Protocol must be approved by the reviewing IRB.

(b) *Informed Consent.* Unless the Biological Sample is anonymized pursuant to Section 21.3.3, if conducting a Genetic Test on a Biological Sample is part of the Research Protocol then such Genetic Test may not be conducted unless consent is obtained using the model form attached as Exhibit 15 or using an

Informed Consent that contains terms materially the same to those found in the model form, from the Human Subject affirmatively consenting to such Genetic Testing for the purposes stated in such consent. This consent is in addition to the general Informed Consent and the Research Authorization Form.

(c) *Sixty Days to Conduct Genetic Testing as part of Research.*

(i) Sixty Day Rule. Generally the Genetic Tests to which the Human Subject has consented must be completed within sixty (60) days from the date of the consent, after which the Biological Sample must be destroyed.¹³⁴

(ii) Extension Past the Sixty Days. With the approval of the IRB and the written consent of the Human Subject, described in Section 21.3.2, the biological sample may be kept for longer than sixty (60) days and utilized for Research purposes.¹³⁵

21.3.2 Content of Consent to Genetic Testing on Biological Samples.

(a) Before any Genetic Test may be conducted on the Biological Sample of a Human Subject, such Human Subject must sign a written consent that includes at least the following:

(i) A general description of the test;

(ii) A statement of the purpose of the test;

(iii) A statement indicating that the individual may wish to obtain professional genetic counseling prior to signing the Informed Consent;

(iv) 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;

(v) A general description of each specific disease or condition tested for;

(vi) The level of certainty that a positive 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;

(vii) The name of the person or categories of persons or organizations to whom the test results may be disclosed;

(viii) A statement that no tests other than those authorized shall be performed on the Biological Sample and that the Biological Sample shall be destroyed at the end of the testing process or not more than sixty (60)

days after the sample was taken, unless a longer period of retention is expressly authorized in the consent; and

(ix) 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.¹³⁶

(b) The requirements of Section 21.3.2(a)(iv), (v) and (vi) may be modified by the IRB in case the Research Protocol does not permit such degree of specificity.¹³⁷

21.3.3 Using Anonymous Biological Samples. Informed Consent is not required for Genetic Tests performed on Biological Samples that have been stripped of all identifiable information and cannot be linked back to a Human Subject through the use of a code or otherwise, provided that the IRB determines that the Research Protocol submitted by the Principal Investigator assures the anonymity of the sources of the samples.¹³⁸

21.3.4 Using Stored Biological Samples for General Research Purposes.

(a) Genetic Tests may be performed on stored Biological Samples for general research purposes (i.e., uses of the biological samples for tests other than those for which specific consent given by individual has been obtained) for genetic testing if:

(i) Each individual providing a Biological Sample gave a written consent to research on the stored samples that is materially the same as the model template found in **Exhibit 15**;

(ii) The individual did not specify any time limits or restrictions on the use of such sample on his or her consent to use the Biological Sample for general research; and

(iii) The samples have been permanently stripped of identifying information, or an IRB-approved coding system has been established to protect the identity of the individuals who provided, or will provide, the samples.¹³⁹

(b) Content of written consent to use stored Biological Samples must contain at least the following:

(i) A statement that the Biological Sample will be used for future genetic tests;

(ii) The time period during which the Biological Sample will be stored, or if no time limit is specified, a statement that the Biological Sample will be stored for as long as deemed useful for Research purposes, accompanied by an explicit check-box allowing the Human Subject to affirmatively “opt-in” to such retention period;

(iii) A description of the policies and procedures to protect Human Subject confidentiality;

(iv) A statement of the right to withdraw, at any time, consent to future use of the Biological Sample, and the name of the organization that should be contacted to withdraw consent; and

(v) A statement allowing individuals to consent to future contact for any or all purposes, including:

(1) Research purposes;

(2) Provision of general information about Research findings;

(3) Information about the test on their sample that may benefit them or their family members in relation to their choices regarding preventative or clinical care; and

(4) An explanation of the benefits and risks of consenting to future contact.¹⁴⁰

It should be noted that the Human Subject may wish to specify a time limit or other restrictions on the use of his or her sample. Anyone conducting Research on any stored Biological Samples should be aware of any such limitations prior to conducting such test.

(c) *Withdrawal of Consent.* If the Human Subject withdraws consent to the storage of his or her Biological Sample at any time, the Principal Investigator should ensure that any portion of the Biological Sample that has not already been used for Research purposes is promptly (but in no event more than sixty 60) days) destroyed.¹⁴¹

(d) *Contact of Human Subject's Relatives.* In no event shall family members of a Human Subject who provided a stored Biological Sample be contacted for clinical, research, or other purposes without consent, as described above, from the Human Subject with respect to the specific family members who will be contacted and the specific purpose of the contact.¹⁴²

21.3.5 Additional Language Regarding Protections under the Genetic Information Nondiscrimination Act.¹⁴³ H+H requires that the following or similar language be placed in any consent for Research in which genetic information will be used or discovered, pursuant to OHRP guidance:¹⁴⁴

"A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- *Health insurance companies and group health plans may not request your genetic information that we get from this research.*
- *Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.*
- *Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.*

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.”

21.3.6 HIPAA Authorization. Regulations promulgated under the Health Insurance Portability and Accountability Act of 1996, while not covering actual specimens, do cover protected health information that may be associated with tissue samples used in genetic testing. Principal Investigators are required to explain to and obtain from the Human Subject both written Informed Consent and a HIPAA authorization before research may commence. For more information on HIPAA authorizations, see the H+H HIPAA Clinical Investigation and Research Policy and Guidelines, Operating Procedure 240-23, Appendix E.

21.3.7 Disclosure of Genetic Testing Information.

(a) *Genetic Testing Information.* Information is Genetic Testing Information if it is information:

- (i) About an individual derived from Genetic Tests, or
- (ii) Linking an individual with specific results of Genetic Tests, to an organization or person, including Principal Investigators or Sponsors.

(b) *Disclosure, General.* Subject to the provisions of Section 21.3.6(c) below, the person at the Facility tasked with the oversight of the privacy of patient and Human Subject information, such as a privacy officer, may determine if a requested disclosure of Genetic Testing Information may be allowed.

(c) *Requirements for Disclosure of Genetic Testing Information.* The disclosure of Genetic Testing information by a Facility or H+H may occur only if the individual from whom the sample was taken has signed a written Research Authorization Form in which such individual:

- (i) Specifically permits such disclosure of genetic information;
- (ii) Identifies the recipient(s); and
- (iii) Identifies the purpose of the disclosure.¹⁴⁵

(iv) (See also H+H HIPAA Clinical Investigation and Research Policy and Guidelines, Operating Procedure 240-23, and OHRP's *Guidance on the Genetic Information Nondiscrimination Act: Implications for Principal Investigators and Institutional Review Boards*).¹⁴⁶

21.3.8 Decedent Data and Genetic Testing.

(a) Where a Principal Investigator seeks to perform genetic testing on decedent specimens, H+H requires that the Principal Investigator seek a special waiver regarding the use of decedent information. H+H requires the completion and submission to the applicable IRB of the Request and Attestation for PHI of Decedents. (See Appendix D of Operating Procedure 240-23, HIPAA Clinical Investigation and Research Policy and Guidelines.)

(b) New York State law requires consent by the next-of-kin of the decedent who is the source of the sample tissue, before genetic testing may be performed.¹⁴⁷

21.3.9 Consent Required for Storage of Biological Samples.

(a) *HIPAA Requirements.* HIPAA considers the act of storing samples in a databank or repository to be Research.¹⁴⁸ Therefore, there are certain steps that must be taken prior to storing and/or using genetic samples for Research purposes. (See also H+H HIPAA Clinical Investigation and Research Policy and Guidelines, Operating Procedure 240-23, Appendix E.)

(b) *Informed Consent.* Prior to the storage of tissue or data in a repository or database/databank, the Principal Investigator must obtain a consent that complies with both New York consent requirements (which are listed in Section 21.3.4(b)) and a HIPAA Research Authorization Form for storage purposes. (See also H+H HIPAA Clinical Investigation and Research Policy and Guidelines, Operating Procedure 240-23, Appendix E.) This consent and authorization is separate and distinct from the Informed Consent and the Research Authorization Form signed by the individual to participate in the Research Project into which he or she is enrolled as a Human Subject. The separate consent to storage and use of tissue for future research permits revocation of such consent to future use by the subject without interrupting the primary Research Project in which he or she is currently enrolled.

(c) *IRB Waiver of HIPAA Research Authorization.* For subsequent use, Research or Research Project of the stored samples, HIPAA requires that the Principal Investigator obtain an additional research authorization for the new use, or a waiver by the IRB of such authorization requirement. Therefore, the IRB may waive this HIPAA requirement. The IRB may not waive the requirements under New York State law. Under those requirements the original consent for Research must include the elements listed under Section 21.3.4(b)). (See also H+H HIPAA Clinical Investigation and Research Policy and Guidelines, Operating Procedure 240-23, Appendix E.)

(d) *Withdrawal of Consent to Storage of Biological Sample.* If consent to storage of a biological sample is withdrawn by the Human Subject at any time, the Principal Investigator, Facility and H+H shall promptly (but in no event more than sixty (60) days) destroy the sample or portions thereof that have not already been used for Research purposes.¹⁴⁹

21.3.10 Storage of DNA Samples. Under New York State Law, retention of a DNA sample for a period of time longer than ten (10) years requires explicit consent for a longer or indefinite storage period.¹⁵⁰ Consent that is materially the same as the model template in **Exhibit 15** must be obtained before Genetic Testing may be performed on the stored sample.

SECTION 22. GUIDELINES FOR USE OF ANATOMICAL GIFTS

22.1 Policy

Under New York State's Uniform Anatomical Gift Law,¹⁵¹ any individual may give all or any part of his or her body for certain purposes by way of a properly executed written authorization for organ or tissue donation.¹⁵²

22.2 Procedures

When H+H, a Facility, Principal Investigator or other researcher is the intended donee for an anatomical gift for research purposes, the gift, its authorization and its terms shall be reviewed by the H+H Office of Research Administration in order to determine the appropriateness of accepting the gift and its use in the Research Project. In addition, such anatomical gift may be reviewed by the corresponding IRB for the Research Project.

PART V

MISCONDUCT, UNANTICIPATED EVENTS & NONCOMPLIANCE

SECTION 23. RESEARCH MISCONDUCT

23.1 Policy

23.1.1 General. H+H prohibits Research Misconduct and requires all Research to comply with applicable law. “Research Misconduct” means Fabrication, Falsification or Plagiarism, as those terms are defined herein, in proposing, performing, or reviewing Research, or in reporting Research results. A finding of Research Misconduct requires all of the following:

- That there be a significant departure from accepted practices of the relevant research community; and
- The misconduct be committed intentionally, knowingly, or recklessly; and
- The Allegation be proved by a Preponderance of the Evidence.

23.1.2 Research Misconduct does not include honest error or differences of opinion. Instances of Research Misconduct may encompass acts that could be construed as violations of federal and state penal laws.

23.1.3 Applicability. This Section 23 applies to allegations of Research Misconduct involving:

(a) All individuals at H+H engaged in Research. This policy applies to any person paid by, under the control of, or affiliated with H+H, such as Principal Investigators, trainees, technicians and other staff members, students, fellows, guest researchers, or collaborators at H+H; and

(b) One of the following:

(i) PHS support biomedical or behavioral research, research training or activities related to that research or research training, such as the operation of tissue and data banks and the dissemination of research information;

(ii) Applications or proposals for PHS support for biomedical or behavioral research, research training or activities related to that research or research training; or

(iii) Plagiarism of Research Records produced in the course of PHS supported research, research training or activities related to that research or research training. This includes any research proposed,

performed, reviewed, or reported, or any Research Record generated from that research, regardless of whether an application or proposal for PHS funds resulted in a grant, contract, cooperative agreement, or other form of PHS support.

23.2 Definitions

For purposes of this Section 23, the following definitions shall apply:

“Allegation” means an allegation of Research Misconduct received through any means of communication that triggers the procedures described by these Policies and Procedures.

“COI Chair” means the individual appointed by the CMO as the head of the Committee of Inquiry.

“Committee of Inquiry” or **“COI”** means the committee appointed by the CMO to determine if an Allegation or apparent instance of Research Misconduct has substance.

“Complainant” means the person who in good faith makes an Allegation of Research Misconduct, including those persons who make Allegations through the H+H Anonymous Reporting Line 866-435-7442 (1-866-HELP-HHC).

“Fabrication” means to forge or devise data or results with subsequent recording or reporting of the forged or devised data.

“Falsification” means manipulating Research materials, equipment, or processes, or changing or omitting data or results such that the Research is not accurately represented in the Research Record.

“Investigation Committee” means the committee appointed by the CMO when a COI determines that the Allegation has substance so as to warrant further investigation.

“ORI” means the U.S. Department of Health and Human Services Office of Research Integrity.

“Plagiarism” is the appropriation of the ideas, processes, results, or words of another person, without giving appropriate credit.

“Preponderance of the Evidence” means proof by information that, compared with that opposing it, leads to the conclusion that the fact at issue is more probably true than not.

“Research Misconduct” means that misconduct described in Section 23.1.1.

“Research Project Data” means all data resulting from the Research Project, including all reports and forms required by the protocol.

“Research Record” includes, but is not limited to, grant or contract applications, whether funded or unfunded; grant or contract progress and other reports; laboratory notebooks; notes; correspondence; videos; photographs; X-ray film; slides; materials; computer files and printouts; manuscripts and publications; equipment use logs; laboratory procurement records; animal facility

records; Research Protocols; consent forms; medical charts; and Human Subject files. The term Research Records excludes rejected grant or contract applications.

“**Respondent**” shall refer to a person or persons accused of Research Misconduct.

23.3 Procedure

23.3.1 Roles and Responsibilities.

(a) *H+H Chief Medical Officer.* The H+H Chief Medical Officer shall be responsible for handling all Allegations of Research Misconduct. The H+H Chief Medical Officer may, during proceedings under these Research Misconduct policies or any subsequent investigation, take whatever administrative actions that are in his or her judgment appropriate to protect public health, research funds or equipment or the legitimate interests of patients. Such administrative actions shall not be deemed disciplinary in nature. Actions may include “stop work” orders, termination of research agreements, locking H+H Facility laboratories, or other appropriate measures, as needed to ensure the integrity of the investigation or patient safety. However, any inquiries from Federal, State and Local law enforcement agencies with respect to alleged Research Misconduct must be promptly directed to the Office of Inspector General in accordance with H+H Operating Procedure 30-1.

(b) *The Coordinator.* The H+H Chief Medical Officer shall designate an individual who serves in the Office of Research Administration to act as a coordinator (“Coordinator”) to assist in carrying out this Section 23. The Coordinator shall act as a neutral facilitator, but shall consult with the H+H Office of Legal Affairs to ensure that the requirements of law and H+H policies and procedures are being satisfied and that any reports or determinations made pursuant to this Policy are legally sufficient. The Coordinator, in addition to assisting the H+H Chief Medical Officer in administering the process of any inquiry or subsequent investigation, shall:

(i) Advise members of the H+H community in response to requests for information or informal consultation concerning Research Misconduct;

(ii) Keep the H+H Chief Medical Officer informed of any Allegations filed and the progress of any inquiry or investigation undertaken;

(iii) Notify the H+H Office of Inspector General of any inquiries from Federal, State and Local law enforcement agencies with respect to alleged Research Misconduct in accordance with H+H Operating Procedure 30-1;

(iv) Work with and advise the various H+H officials and committees involved in the inquiry and/or any subsequent investigation or

disciplinary action. The Coordinator shall offer advice regarding H+H rules and policies governing the process;

(v) Assist the appropriate officials and committees in carrying out the inquiry and/or any subsequent investigation, including assembling evidence and conducting interviews;

(vi) Notify the IRB of any Allegation;

(vii) Be responsible for communications with any person or organization outside H+H having a legitimate interest in the case, including any funding agency;

(viii) Notify ORI and the applicable Federal funding entities if he/she, along with the H+H Chief Medical Officer, believes that any of the following conditions exist:

(1) Health or safety of the public is at risk, including an immediate need to protect Human Subjects;

(2) Federal resources or interests, including funds or equipment, are threatened;

(3) Research activities should be suspended, as determined through this evaluation and in conjunction with the IRB;

(4) There is indication of possible violations of civil or criminal law;

(5) Federal action is required to protect the interests of those involved in the Research Misconduct proceeding;

(6) H+H determines that the Research Misconduct proceeding may be made public prematurely so that the Federal oversight agency may take appropriate steps to safeguard evidence and protect the rights of those involved; or

(7) The research community or public should be informed.

(ix) Contact the following H+H offices for further instruction:

(1) Upon any indication that an instance of Research Misconduct may have violated any civil laws, contact the Office of Legal Affairs and Office of Corporate Compliance for further instructions.

(2) Upon any indication that an instance of Research Misconduct may have violated any criminal laws, contact the Office of Inspector General for further instruction.

(3) Refer the matter to the Chief Medical Officer and cooperate with and assist in coordinating any related actions or inquiries when, in the course of an inquiry or subsequent investigation, other H+H policies are implicated. The Coordinator will consult with the Offices of Legal Affairs and Corporate Compliance.

(x) Maintain objectivity regarding the veracity of the Allegations throughout the proceedings. The Coordinator shall serve as a neutral facilitator, and shall not assume the role of a prosecutor or judge;

(xi) File an annual report with the ORI, which contains information specified by ORI on institutional compliance with Federal regulations on Research Misconduct; and

(xii) Cooperate fully with ORI during its oversight review and any subsequent administrative hearings or appeals, including providing all Research Records and evidence under H+H's control, custody, or possession and access to all persons within its authority necessary to develop a complete record of relevant evidence.

23.3.2 Initiation of Complaint.

(a) *Filing of Allegation.* Allegations of Research Misconduct may be filed with the Chief Medical Officer, the applicable Facility Executive Director, or directly with the Coordinator or with the H+H Anonymous Reporting Line 866-435-7442 (1-866-HELP-HHC).

(i) Informal requests for information or consultation concerning Research Misconduct will not, in and of themselves, be construed as formal charges of misconduct.

(ii) Allegations of Research Misconduct shall be immediately referred to the Coordinator who will consult the Office of Legal Affairs for further guidance. If Allegations are filed against more than one individual, a separate process shall be undertaken and decision will be reached for each individual.

23.3.3 Assessment of Allegations.

(a) *Assessment Procedure.*

(i) When Allegations are filed, the Coordinator shall determine if the Allegation meets the criteria of Research Misconduct as defined in

Section 23.1.1. The Coordinator may consult with the appropriate individuals from the applicable Facility so that potential evidence of Research Misconduct may be identified and preserved.

(ii) The Coordinator shall investigate the information or circumstances giving rise to the Allegation. He/she may further consult with the Office of Legal Affairs.

(iii) If the Respondent is consulted during the preliminary review, he/she shall be given an opportunity to review the Allegation and to consult with advisors, if he/she desires, prior to discussing the Allegation with the Coordinator. The Respondent should be informed that the H+H Office of Legal Affairs serves as an advisor to H+H and cannot render legal advice to the Respondent.

(b) *Protecting Data.*

(i) The Coordinator shall take immediate action to protect data or other materials relevant to the accusation. Under the direction of the Coordinator, the H+H Facility Executive Director shall, prior to notifying Respondent of the Allegations, take all reasonable and practical steps to obtain custody of, inventory and sequester in a secure manner all Research Records and evidence needed to conduct the Research Misconduct proceeding, in accordance with 42 C.F.R. § 93.305.

(ii) The need for additional sequestration of records for the investigation may occur for any number of reasons, including H+H's decision to investigate additional allegations not considered during the inquiry stage or the identification of records during the inquiry process that had not been previously secured.

(iii) Supervised access to the Research Records and other materials shall be provided to the investigative bodies looking into the Allegation, to the Respondent, and any other person who has a legitimate reason which is related to the investigation, to have access.

(c) *Allegations that Fail to Indicate Possible Misconduct.*

(i) Dismissal of Allegations. If the Coordinator finds that an Allegation does not fit within the definition of Research Misconduct, or the Allegation is not sufficiently credible or specific so that potential evidence of Research Misconduct may be identified, the CMO shall dismiss the Allegation in writing and notify the Complainant of such dismissal in writing.

(ii) Appeal of Dismissal of Allegations. The dismissal shall be a final determination of the Allegation unless, within one week of receiving the dismissal, the Complainant appeals in writing to the CMO. Promptly

after receipt of the appeal, the CMO should reach a decision regarding whether to affirm the dismissal or to send the Allegation for further review to the appropriate parties. The decision of the CMO shall be final. If an Allegation has been dismissed but may constitute a violation of another H+H policy or procedure, the Coordinator shall direct the Complainant to the Offices of Legal Affairs and/or Corporate Compliance.

(d) *Allegations Indicating Possible Misconduct.* If the Coordinator or the Chief Medical Officer determines that the Allegation meets the definition of Research Misconduct in Section 23.1.1 and is sufficiently credible and specific so that potential evidence of Research Misconduct may be identified, the Coordinator shall reduce the Allegation to writing and provide the Respondent with the written description of the Allegation. The Coordinator shall meet with the Respondent to inform him/her of the following:

(i) The Allegation, in detail, and the procedures for handling such Allegations detailed herein;

(ii) The obligation under this Section 23 to cooperate with the investigation process and to provide documentary evidence requested; and

(iii) The nature of the Allegations, the consequences that could result, and the right to consult legal counsel or other appropriate advisors regarding the matter.

23.3.4 Inquiry.

(a) *General.* If the Coordinator, or the CMO, determines that the Allegation indicates possible Research Misconduct, an inquiry shall be immediately initiated. The purpose of the inquiry is to conduct preliminary information-gathering and preliminary fact-finding to determine if an Allegation or apparent instance of Research Misconduct has substance. If an allegation has substance, then an investigation is warranted.

(b) *The Committee of Inquiry.*

(i) Committee Appointment. The CMO shall form a Committee of Inquiry (“COI”) and appoint a COI Chair. The COI Chair shall inform the Respondent in writing of the names of those appointed as COI members and as consultants.

(ii) Committee Membership. In making appointments to the COI, the CMO shall appoint at his or her discretion individuals with the following qualifications:

(1) Individuals with appropriate scientific and/or academic expertise to evaluate the evidence and issues related to the Allegation;

(2) Individuals free from bias and any real or apparent personal, professional or financial conflicts of interest with the Complainant or Respondent;

(3) At least one individual who has acted as the Principal Investigator for a Research Project in the last five (5) years. This individual(s) cannot be affiliated with the Facility at which the Allegation has occurred;

(4) The Coordinator shall serve as a neutral advisor to the COI to assist in facilitating the inquiry and advising the COI as to issues of process and procedures; the Coordinator shall have no vote on the decisions reached by the COI and shall not influence discussions concerning whether the case has substance.

(iii) Opportunity to Object. The Respondent may, within one week of receiving the names of COI members, file a written objection with the COI Chair. Such objection may be based on grounds of a lack of the requisite expertise or possible personal, professional, or financial conflicts of interest. The COI Chair shall promptly rule on such objections and, if they are found to have merit, the COI shall be reconstituted.

(c) *Conducting the Inquiry.* The COI shall collect and review preliminary evidence and interview individuals having relevant information, including the Respondent, which supports or refutes the Allegations, with the objective of determining whether the Allegation has substance. The Respondent shall be kept informed of the evidence and the substance of the interviews and shall be furnished with or have access to copies of all documentary evidence. However, the Respondent shall not have the right to be present when witnesses are interviewed or to question such witnesses at this stage of the proceeding. The Respondent may submit any relevant evidence for consideration by the COI. The Inquiry shall be completed within sixty (60) days of its initiation unless circumstances clearly warrant a longer period.

(d) *Scope.* During the initial inquiry, additional information may emerge that justifies broadening the scope of the inquiry beyond the initial Allegation. By majority vote of the COI, the scope of the inquiry may be broadened when the additional evidence relates directly to the instance of Research Misconduct currently being investigated. The Respondent must be promptly informed in writing of any such decision and of the nature of the broadened scope.

(e) *Preliminary and Final Inquiry Reports.*

(i) When the COI has reached a conclusion on whether or not the Allegations have substance, it shall prepare a preliminary report that sets forth the name and position of the Respondent, a description of the Allegation, a description of any known Federal Research support, the names of COI members and any non-voting consultants, a list of the documentary

evidence reviewed, summaries of any interviews, and the basis for finding or not finding that the Allegation has substance, as well as the determination by the COI whether an investigation is warranted (a "Preliminary Inquiry Report").

(ii) H+H will notify the Respondent and Complainant (providing relevant portions of the report to the Complainant for comment) whether the inquiry found that an investigation is warranted. The notice must include a copy of the Preliminary Inquiry Report and include a copy of or refer to 42 C.F.R. Part 93 and this policy. The Respondent may, within two weeks of receiving the Preliminary Inquiry Report, file with the COI a written response. If such a response is filed, the COI shall reconsider its conclusion in light of the response and issue a final written decision.

(iii) The decision, along with copies of the Preliminary Inquiry Report and the written response of the Respondent, shall constitute the final report entitled "Final Inquiry Report" and shall be forwarded to the CMO, Respondent, and Complainant.

(f) *Notification to ORI.* Within thirty (30) days of finding that an investigation is warranted, and prior to the initiation of the formal investigation, H+H must provide ORI with the written finding by the responsible institutional official and a copy of the final inquiry report, which must include the following elements:¹⁵³

(i) The name and position of the respondent;

(ii) A description of the Allegations of Research Misconduct;

(iii) The PHS support, including, for example, grant numbers, grant applications, contracts, and publications listing PHS support;

(iv) The basis for recommending that the alleged actions warrant an investigation; and

(v) Any comments on the report by the Respondent or the Complainant.

(g) *Allegations Having Insufficient Substance.*

(i) Inquiry Dismissal. If the COI determines in its preliminary report that the Allegations do not have sufficient substance to warrant an investigation under the disciplinary rules of H+H, the case shall be dismissed, unless, within one week of receiving the final decision, the Complainant appeals that determination in writing to the CMO.

(ii) Appeal of Inquiry Dismissal. The CMO shall promptly rule on the appeal and provide written notice of his or her decision to the COI,

Respondent, and Complainant. If the CMO affirms the decision of the COI, the case shall be dismissed. A written notice of the conclusion reached after reconsideration shall be provided to the Respondent and Complainant. The records will be kept for seven (7) years after the termination of the inquiry.

(h) *Allegations Having Sufficient Substance.*

(i) Communications with Parties: Appeals. If the COI determines in its final report that the Allegations have sufficient substance to warrant an investigation under the disciplinary rules of H+H, the Respondent may appeal this decision in writing to the CMO within one (1) week of receiving notice of the decision. The CMO shall promptly rule on it and provide written notice of his or her decision to the COI, Respondent, and Complainant.

The CMO may not reverse the decision of the COI but may refer the matter back to the COI for reconsideration. A written notice of the conclusion reached after reconsideration shall be provided to the Respondent and Complainant. If the COI decides upon reconsideration that the case shall be dismissed, that decision shall be final. If the CMO denies the appeal, the COI Chair shall refer the case, the final report of the COI, and all relevant supporting evidence to the appropriate disciplinary body.

(ii) Report to Sponsor. If the COI has determined in its Final Inquiry Report that an Allegation has sufficient substance to warrant an investigation under the disciplinary rules of H+H, the Coordinator shall inform any sponsoring entity of the Allegations as required by contract or law and shall keep the entity informed as appropriate. If the Allegation involves the Public Health Service (PHS) or National Science Foundation (NSF) funded Research, the Coordinator must provide written notice to the ORI (for PHS-funded research), to the U.S. Office of Inspector General for NSF-funded research, or to any other applicable Federal regulatory agency. Others affected by the Allegations, such as co-authors or co-investigators, shall be informed of the proceedings.

23.3.5 Investigation. When a COI determines that the Allegation has substance through the inquiry process described in Section 23.3.4, an investigation will be initiated. Such investigation and any disciplinary sanctions, if necessary, shall comply with H+H policy and practice, as well as with this Section 23 and 42 C.F.R. Part 93.

(a) *Investigation Committee.*

(i) Committee Appointment. An Investigation Committee shall be appointed by the CMO. The CMO shall designate a Chair of the Investigation Committee. The Investigation Committee Chair shall inform the Respondent in writing of the names of those appointed as Investigation Committee members.

(ii) Committee Membership.

(1) The Investigation Committee shall consist of:

- a. The RA Director;
- b. At least one individual who has acted as the Principal Investigator for a Research Project in the last five (5) years who is not affiliated with the Facility at which the Allegation has occurred; and
- c. Any other persons inside or outside H+H, at the CMO's discretion, with the following qualifications:
 - i. Individuals with appropriate scientific and/or academic expertise to evaluate the evidence and issues related to the Allegation;
 - ii. Individuals free from bias and any real or apparent personal, professional or financial conflicts of interest with the Complainant or Respondent.

(2) Qualified individuals who have served on the COI Committee may serve on the Investigation Committee, provided that the total number of COI Committee Members does not constitute more than 50 percent of the total Investigation Committee membership.

(3) The Coordinator shall serve as a neutral advisor to the COI to assist in facilitating the investigation and advising the Investigation Committee as to issues of process and procedures; the Coordinator shall have no vote on the decisions reached by the Investigation Committee and shall not influence discussions concerning whether the case has substance. The CMO shall not be a member of the Investigation Committee but should be available for advice if any member of the Investigation Committee requests consultation.

(iii) Opportunity to Object. The Respondent may, within one (1) week of receiving the names of Investigation Committee members, file a written objection with the Investigation Committee Chair. Such objection may be based on grounds of a lack of the requisite expertise or possible personal, professional, or financial conflicts of interest. The Investigation Committee Chair shall promptly rule on such objections and, if they are found to have merit, the Investigation Committee shall be reconstituted.

(b) *Preliminary and Final Investigation Reports.*

(i) A preliminary investigation report shall be prepared by the Investigation Committee and include the following: a description of the Allegations of Research Misconduct; a description of any Federal Research support; the name of the Respondent, the names of the Investigation Committee and any consultants; a list of the documentary evidence reviewed and interview summaries; and a statement of the findings, the conclusions reached, and the recommended sanctions (a "Preliminary Investigation Report"). The Preliminary Investigation Report shall be forwarded to the Respondent, the Complainant, and the CMO.

(ii) The Respondent shall be provided with a copy of the Preliminary Investigation Report and concurrently a copy of, or supervised access to, the evidence on which the report is based. The Respondent shall have thirty (30) days from the date he/she receives a copy of the Preliminary Investigation Report and a copy of, or access to the evidence, to provide written comments on the Preliminary Investigation Report.

(iii) A final investigation report will be prepared and consist of the preliminary investigation report, the comments of the Respondent and Complainant, if any, and any additional findings of the Investigation Committee and all other information and elements required by 42 C.F.R. § 93.313 (a "Final Investigation Report"). The Final Investigation Report shall be forwarded to the Respondent, the Complainant, and the CMO. The CMO shall forward the report to the relevant oversight agency or funding entity. All records of Research Misconduct proceedings shall be retained in accordance with 42 C.F.R. § 93.317.

(c) *Timing of Investigation and Reports.* Unless ORI grants an extension in writing, the investigation must be complete within 120 days of beginning it, including conducting the investigation, preparing the Preliminary Investigation Report, providing a copy of the preliminary investigation report for comment to the Respondent and sending the Final Investigation Report to ORI.

23.3.6 Sanctions. Appropriate sanctions shall be imposed by H+H when a final investigation report finds that Research Misconduct has occurred. Sanctions shall be commensurate with the severity of the Research Misconduct.

23.3.7 Notice to ORI of Findings and Actions. H+H must provide ORI with the following:

(a) Final Investigation Report, including a copy of the report, all attachments, and any appeals;

(b) A statement of whether H+H found Research Misconduct, and if so, who committed the misconduct;

(c) A statement as to whether H+H accepts the investigation's findings;
and

(d) A description of any pending or completed administrative actions
against the Respondent.

23.3.8 Correction of Erroneous Research. If Research Misconduct has been found under Section 23.3.5 and erroneous Research Project Data has been published, the Respondent will work with H+H and any other researchers or publishers involved to correct the published record. If no Research Misconduct has been found but seriously erroneous research has been published, H+H, working with the researchers involved, will seek to correct the published record.

23.3.9 Evidence of Criminal Conduct. If any individual involved in an inquiry or subsequent investigation becomes aware of a possible violation of criminal or civil law, he or she shall refer the matter immediately to the H+H Office of Inspector General in accordance with H+H Operating Procedure 30-1.

23.3.10 Time Limitations. The requirements set forth in this Section 23 apply only to Research Misconduct occurring within six (6) years of the date H+H or a federal sponsor or oversight agency receives an Allegation of Research Misconduct. Exceptions to the six-year year limitation include the following:

(a) *Subsequent Use.* The Respondent continues or renews any incident of alleged Research Misconduct that occurred before the six-year limitation through the citation, republication or other use by the Respondent of the Research Record that is alleged to have been fabricated, falsified, or plagiarized.

(b) *Health or safety of the public exception.* If H+H, following consultation with the Federal sponsor or oversight agency, determines that the alleged Research Misconduct, if it occurred, would possibly have a substantial adverse effect on the health or safety of the public.

(c) *"Grandfather" exception.* If the Federal sponsor or oversight agency or H+H received the Allegation of Research Misconduct before the effective date of these Policies and Procedures.

23.3.11 Retaliation. The Complainant may request anonymity; however the ability to keep a Complainant's identity anonymous will depend on the type of allegation he/she is making, and the specific facts and circumstances involved in the Allegation. The process within H+H does require that the Complainant be identified as the 'complainant' but H+H will strictly limit disclosure of his/her identity, as well as that of the Respondent, to those who need to know in order to carry out a fair, thorough and objective proceeding. Any records or evidence that may convey the identity of others will also be kept confidential, except as otherwise required by law.

H+H must undertake all reasonable and practical efforts to protect the positions and reputations of good faith Complainants, witnesses, and committee members and protect them from retaliation by the Respondent and others. Documented retaliation by the Respondent or other H+H employees

against good faith Complainants, witnesses or committee members shall result in disciplinary action under appropriate H+H rules, policies or procedures.

23.3.12 Confidentiality. H+H and anyone involved in a Research Misconduct investigation shall:

(a) Limit disclosure of the identity of Respondents and Complainants to those who need to know in order to carry out a thorough, competent, objective and fair Research Misconduct proceeding; and

(b) Except as otherwise prescribed by law, limit the disclosure of any records or evidence from which Human Subjects might be identified to those who need to know in order to carry out a Research Misconduct proceeding.

23.3.13 Restoration of the Respondent's Reputation. Following a final finding that Research Misconduct did not occur, H+H will undertake all reasonable and practical efforts to restore the Respondent's reputation. Such efforts may include notifying those individuals aware of or involved in the investigation of the final outcome, publicizing the final outcome in any forum in which the Allegation of Research Misconduct was previously publicized, and deleting all reference to the Research Misconduct Allegation from the Respondent's personnel file. Any actions to restore the Respondent's reputation should first be approved by the H+H Chief Medical Officer.

SECTION 24. PROTOCOL VIOLATIONS AND DEVIATIONS

24.1 Policy

H+H requires all Major Protocol Deviations and Major Protocol Violations to be reported as set forth below.

24.2 Definitions

For purposes of this Section 24, the following definitions shall apply.

“Major Protocol Deviation” means a Protocol Deviation that is likely to affect the outcome, analysis or interpretation of the Research Project. The criteria for major deviations may vary and is frequently defined by the local IRB or protocol, but often include factors having a significant impact on consent, eligibility, treatment, reporting of toxicity, participant risk and safety, disease outcome, regulatory compliance and data quality.

“Major Protocol Violation” means a violation that is likely to impact subject safety, affect the integrity of Research Project Data and/or affect subject's willingness to participate in the Research Project.

“Protocol Deviation” means a departure from the Research Protocol procedures approved by the IRB that was made by the Principal Investigator without prior IRB approval.¹⁵⁴ Please note: eligibility exceptions (or eligibility waivers granted by a Sponsor) for enrollment of a specific

individual who does not meet the inclusion/exclusion criteria in the IRB approved Research Protocol are not deviations. Eligibility exceptions are considered changes in a Research Project that require IRB review and approval before a Human Subject who does not meet the approved Research Protocol inclusion/exclusion criteria may be enrolled.

“**Protocol Violation**” means any intended or unintended variance, exception or deviation from the IRB-approved Research Protocol.¹⁵⁵

24.3 Procedures

24.3.1 Protocol Violations. All Major Protocol Violations that occur in an H+H Facility must be reported by the Principal Investigator to the Office of Research Administration, the Medical Director and applicable IRB in accordance with the timeframe and process set forth in the IRB’s policies and procedures.

24.3.2 Protocol Deviations. All Protocol Deviations, including Major Protocol Deviations, and Protocol Violations should be reported to the applicable IRB in accordance with the timeframe and process set forth in the applicable IRB’s policies and procedures. The IRB is responsible for reporting such incidents to H+H.

24.3.3 Changes to Protocol. Changes to a Research Protocol that are necessary to immediately protect the safety of Human Subjects or others may be initiated without prior IRB or H+H approval.¹⁵⁶ Any such changes should be reported to the IRB as soon as possible after they occur.

24.3.4 Other Reporting Requirements. Sponsor or Grantor reporting requirements for such deviations may differ from Affiliate reporting requirements. Principal Investigators should be aware that agreements entered into with the Sponsor or Grantor with respect to a Research Project may require the Principal Investigator to notify the Sponsor or Grantor of all Protocol Violations, including unplanned deviations or departures from IRB-approved protocol procedures. It is the Principal Investigator’s responsibility to comply with the reporting requirements outlined in the signed contract or protocol with the Grantor or Sponsor. Before a Principal Investigator acknowledges and agrees to the terms of a Research agreement, the Principal Investigator is strongly advised to read and understand the contract terms, working with the Office of Research Administration and/or H+H’s Office of Legal Affairs which will promptly advise Principal Investigators, as needed, prior to signing. Final approval will be obtained from the Office of Research Administration and the Office of Legal Affairs.

SECTION 25. REPORTING OF UNANTICIPATED PROBLEMS

25.1 Policy

25.1.1 H+H is required to have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials and any supporting department or agency head of any Unanticipated Problem Involving Risks to Human Subjects or Others.¹⁵⁷ Accordingly, H+H requires Principal Investigators to promptly report all Unanticipated Problems and all Serious Adverse Events that occur at an H+H Facility as set forth below.

25.1.2 Unanticipated Problem Involving Risks to Human Subjects or Others, in general, include any incident, experience, or outcome that occurs as a result of a Human Subject's participation in Research that meets all of the following criteria:

- (a) Unexpected (in terms of nature, severity, or frequency) given
 - (i) The Research Project procedures that are described in the protocol-related documents, such as the IRB-approved Research Protocol and Informed Consent document; and
 - (ii) The characteristics of the Human Subject population being studied;
- (b) Related or possibly related to participation in the Research Project (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the Research Project procedures); and
- (c) Suggests that the Research Project places Human Subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

25.2 **Definitions**

For purposes of this Section 25, the following definitions shall apply.

“Adverse Event” means any untoward or unfavorable medical occurrence in a Human Subject, including any abnormal sign, physical examination, laboratory finding, symptom, disease, temporarily associated with the Human Subject's participation in Research, whether or not considered related to the Human Subject's participation in Research, as set forth by the applicable IRB or in the Research Protocol. An Adverse Event includes both internal and external events, any undesirable sign, symptom or medical or psychological condition even if the event is not considered to be related to the investigational drug/device/intervention. Medical condition/diseases present before starting the investigational drug/device/intervention will be considered Adverse Events only if they worsen after starting Research Project treatment/intervention. An Adverse Event is also any undesirable and unintended effect of Research occurring in Human Subjects as a result of the collection of private information as part of the Research Project that may be used to identify such Human Subject. Adverse Events also include any problems associated with the use of an Investigational Device that adversely affects the rights, safety or welfare of Human Subjects.¹⁵⁸

“Related” means associated with, having a timely relationship with, or a reasonable possibility exists that an outcome may have been caused or influenced by the event in question (e.g., administration of a study drug); although an alternative cause/influence may also be present. Related events include incidents that are definitely, probably, or possibly related.

“Serious Adverse Event” means an adverse event that is fatal or life threatening, permanently disabling, requires inpatient hospitalization or prolongs existing hospitalization, or results in

persistent or significant disability or incapacity, congenital anomaly, or birth defect or based on medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this paragraph, as set forth by the applicable IRB or in the Research Protocol.

“Unanticipated Problem Involving Risks to Human Subjects or Others” or “Unanticipated Problems” means those events described in Section 25.1.2.

“Unrelated” means unassociated or without a timely relationship, or when conclusive evidence exists that an outcome is definitely related to a cause other than the event in question.

25.3 Procedures

25.3.1 Determining Whether an Event is Reportable. Whether an event constitutes an Unanticipated Problem Involving Risks to Human Subjects or Others or a Serious Adverse Event should be determined by the Principal Investigator together with the Sponsor or Grantor (if the applicable Research Protocol or agreement requires joint determination), protocol team or by an appropriately designated committee. This determination is subject to review by the applicable IRB. Principal Investigators should adhere to the policy of the IRB overseeing a Research Project with regard to timely reporting required events.

25.3.2 Events that Should be Reported Promptly. The following events may represent Unanticipated Problems Involving Risks to Human Subjects or others and thus should be promptly reported to the Office of Research Administration, Medical Director, Facility Research Administration Office, and applicable IRB in accordance with the timeframe and process set forth in the IRB's policies and procedures:

- (a) Adverse device effects that are unanticipated;
- (b) Adverse Events or injuries that are serious and unexpected and related;
- (c) Breaches of confidentiality;
- (d) Data and Safety Monitoring Board (DSMB) reports, interim analyses, or other oversight committee/monitoring reports altering the risk/benefit profile;
- (e) Events requiring prompt reporting according to the Research Protocol, Sponsor or Grantor;
- (f) Investigator's brochure updates/revisions to safety information (excluding routine updates; New information indicating an unexpected change in risks or potential benefits (e.g., literature/scientific reports or other published findings);
- (g) Protocol deviations, violations, or other accidental or unintentional changes to the Research Protocol or procedures involving risks or with the potential

to recur (See Section 24 of these Policies and Procedures for further information on Protocol Deviations and Violations);

(h) Human Subject complaints indicating an unanticipated risk, or complaints that cannot be resolved by the Research Project staff;

(i) Unapproved changes made to the Research Project to eliminate an apparent immediate hazard to a Human Subject;

(j) Other problem or finding (e.g., loss of Research Project Data or forms, a Human Subject becomes a prisoner while participating in Research, etc.) that an investigator or Research Project staff member believes could influence the safe conduct of the Research.

25.3.3 Events Which are Not Immediately Reportable. Potential risks and adverse events occurring at an H+H Facility that may be reasonably anticipated (i.e., “expected”) may not be immediately reportable to the IRB, but should be described in the Informed Consent process/form and reported in accordance with IRB policies and procedures. The following are examples of events that may not require prompt reporting:

(a) Adverse Events or injuries that are non-serious, expected, or unrelated;

(b) Deaths not attributed to the Research Project, e.g., from “natural causes,” accidents, or underlying disease and the investigator has ruled out any connection between the Research Project procedures and Human Subject’s death;

(c) DSMB reports; interim analyses; or other reports, findings, or new information not altering the risk/benefit profile;

(d) Investigator’s brochure updates not involving safety information;

(e) Protocol deviations or violations unlikely to recur or not involving risks to Human Subjects;

(f) Human Subject complaints that were resolved or complaints not involving risks;

(g) Problems or findings not involving risk (unless the investigator or Research Project staff member believes the information could affect Human Subject’s willingness to continue in the Research Project).

25.3.4 Parallel Reporting Requirements.

(a) *Institutional Reporting.*

(i) The Office of Research Administration, in accordance with the terms of H+H’s Federalwide Assurance, will ensure that OHRP, FDA (as applicable for FDA-regulated Research Projects) and the Sponsor or

Grantor as necessary, are notified of Unanticipated Problems Involving Risks to Human Subjects or others within thirty (30) days.

(ii) The Facility Research Administration Offices will ensure that any other department or individual within the Facility and H+H, including, but not limited to, the Office of Risk Management and the Office of Corporate Compliance, is notified in order to satisfy any additional reporting requirements, as applicable.

(b) *Breaches of Confidentiality.* Although a breach of confidentiality or privacy may be considered an Unanticipated Problem, and thus reportable to the IRB, any such breach must also be reported directly to the Facility Research Privacy Officer immediately in accordance with H+H's HIPAA Clinical Investigation and Research Policy and Guidelines, Operating Procedure 240-23. The Facility Research Privacy Officer will work in conjunction with the Facility's compliance division or H+H's Office of Compliance as necessary to mitigate and manage any such breach.

(c) A breach of confidentiality includes, but is not limited to, any computer data security breach (i.e., lost or stolen computer/laptop and/or removable media used as storage devices, such as a flash drive or CD) on which personally identifiable information may have been or be acquired by an unauthorized person.

SECTION 26. REPORTING NONCOMPLIANCE

26.1 Policy

Federal regulations require that H+H has written procedures for ensuring prompt management of any instances of serious or continuing non-compliance with OHRP policy.¹⁵⁹ Any member of the Research Team who observes or otherwise becomes aware of apparent serious or continuing non-compliance with these Policies and Procedures or applicable Federal, State, and Local laws and regulations or the requirements or determinations of the IRB or H+H in connection with Research, has the duty and responsibility to report such noncompliance to the FRRC Chair, IRB and appropriate institutional officials.¹⁶⁰ H+H will facilitate the review of any allegations in a timely manner and, to the extent possible, in a manner that is protective of both the individual(s) that have reported the alleged violation and those that are the subject of the alleged violation.

26.2 Procedure

26.2.1 *Reporting Non-Compliance.*

(a) Instances of possible serious or continuing non-compliance with respect to Research must be reported to the applicable IRB and to the Office of Research Administration. The Office of Research Administration Research number is 212-788-2181.

(b) Instances of misconduct that involve breaches of confidentiality, privacy and data security issues, or inappropriate or improper record management practices, must be reported to the Office of Corporate Compliance. The Office of Compliance's confidential helpline is 866-435-7442 (1-866-HELP-HHC).

(c) Instances of conduct involving fraud, abuse, and waste with respect to billing, coding, and time and effort reporting, must be reported to the Office of Research Administration, Office of Compliance, and should also be simultaneously reported to the IRB. The Office of Compliance's confidential helpline is 866-435-7442 (1-866-HELP-HHC).

(d) Instances of conduct involving non-compliance that might be criminal in nature must be reported to the Office of Research Administration and the H+H Office of Inspector General, and should also be simultaneously reported to the IRB. The Office of Inspector General Hotline is 212-676-0942.

26.2.2 Verbal Reports. If a verbal report is received, the individual who made such report may be required to subsequently submit a written report.

26.2.3 Investigation. All allegations will be promptly investigated by the Office of Research Administration, Office of Compliance, Office of Inspector General or Office of Legal Affairs, as applicable depending on the nature of the non-compliance reported as discussed above. The results of such investigation shall be documented.

26.2.4 Confidentiality. All matters will be reviewed confidentially to the extent possible and as warranted by the situation.

SECTION 27. NON-RETALIATION AND PROTECTION OF WHISTLEBLOWERS

27.1 Policy.

No member of the Research Team or other individual employed by, on staff at, or otherwise affiliated with H+H shall be discriminated against or be subject to reprisal for reporting any instance of alleged non-compliance under these Policies and Procedures or research misconduct. Any attempt to intimidate or retaliate against a person for reporting such issues may itself be considered serious non-compliance with H+H policies and procedures, and will result in disciplinary in accordance with H+H policies and procedures.

27.2 Procedure.

No additional procedure, outside of what has been identified above.

PART VI

RESEARCH RECORDS, REIMBURSEMENT, COSTS & REPORTING

SECTION 28. RESEARCH RECORDS

28.1 Policy.

In order to ensure that H+H patients are given the best possible clinical care, it is imperative that researchers maintain Research Records in a way that alerts treating physicians of a Human Subject's participation in a Research Project. In addition, as Research Records of Human Subjects are the property of H+H, H+H is responsible for maintaining and providing access to Research Records in accordance with its contracts with Sponsors and Grantors and applicable law.

28.2 Definitions.

For purposes of this Section 28, the following definitions shall apply:

“Research Project Data” means all data resulting from the Research Project, including all reports and forms required by the protocol.

“Research Record” includes, but is not limited to, grant or contract applications, whether funded or unfunded; grant or contract progress and other reports; laboratory notebooks; notes; correspondence; videos; photographs; X-ray film; slides; materials; computer files and printouts; manuscripts and publications; equipment use logs; laboratory procurement records; animal facility records; Research Protocols; consent forms; medical charts; and Human Subject files. The term Research Records excludes rejected grant or contract applications.

28.3 Procedures.

28.3.1 All Research Records shall contain all information required by law.¹⁶¹

28.3.2 If a patient is taking part in a Research Project involving a drug, device, or procedure (therapeutic trial), the patient's participation must be clearly noted in the patient's electronic medical record. Researchers should scan and upload Informed Consent forms into the electronic medical record when and where possible, preferably to a research folder. Research Records related to an FDA application must be maintained in accordance with FDA requirements.

28.3.3 Where a contract between H+H and a Sponsor or Grantor requires H+H to retain Research Records for a period that is longer than that required by law, H+H will adhere to that contractual retention period.

28.3.4 Principal Investigators or their designee shall include all Research Project Data in the Research Record along with source documents.

28.3.5 All Research Records must be maintained and disposed of in accordance with applicable provisions of H+H Operating Procedure 120-19, H+H record management policies, and applicable law.

28.3.6 In addition to the foregoing, the Facility must retain Research Records¹⁶² for seven (7) years after the termination of the Research Project or one (1) year after the youngest Human Subject attains age 21, or the date of the last disclosure of identifiable health information from Research Records, if disclosures continue after all subjects have completed the Study, whichever is longer,¹⁶³ and must make them available to H+H, upon request, in a manner that is consistent with the confidentiality and rights of the Human Subjects. (Please see H+H HIPAA Clinical Investigation and Research Policy and Guidelines, at Sections 8.0 through 8.2 and 9.0, and H+H Operating Procedure No. 120-19: Guidelines for Corporate Record Retention and Disposal, for more information regarding additional duties in connection with document retention and accounting of disclosures.)

28.3.7 Research Records used in any regulatory or legal matter must be retained in accordance with H+H Operating Procedure No. 120-19. However, prior to disposing of Research Records, the Office of Legal Affairs and the Office of Corporate Compliance must be consulted to verify that a regulatory or legal matter has not been initiated and that there is no other longer retention period that applies to the Research Record(s) at issue.

28.3.8 Research Records at H+H must be accessible for inspection and copying by authorized representatives of DHHS at reasonable times and in a reasonable manner.¹⁶⁴

28.3.9 Where an Affiliate or unaffiliated entity is the Grantee, the responsible IRB and Grantor or Sponsor, as well as OHRP and the FDA, each have the right to inspect any and all Research Records that are under its jurisdiction, subject to applicable privacy and confidentiality laws and regulations and a written authorization obtained from the Human Subject.

28.3.10 Copies of the signed HIPAA authorization form or combined HIPAA authorization form and Informed Consent (and proof of minor's assent, where appropriate) required under the Common Rule¹⁶⁵ and FDA human subject regulations, as well as New York State consent forms for research and/or testing regarding specially protected health information, such as information pertaining to HIV-AIDS status, genetics, mental health and substance use treatment, are to be kept in the Human Subject's research folder and become a permanent part thereof.

28.3.11 Any contract between H+H and a vendor for a Research Record management system must be first approved by the Office of Corporate Compliance for purposes of ensuring compliance with applicable state and New York City data storage requirements.¹⁶⁶

SECTION 29. HUMAN SUBJECT AS INPATIENT OR OUTPATIENT

29.1 Policy

With the exception of admissions for specified and approved Research services and admissions for Human Subject injury, Human Subjects may be admitted to inpatient or outpatient units of H+H facilities solely for Research purposes only if the Research Protocol has been specifically approved for such admission or extension of stay. Unless waived by the Facility Executive Director, any such admission or extension of hospitalization for Research purposes must be fully reimbursed to H+H.

29.2 Procedure

The Research Project must be identified at the time of the encounter and related reimbursement methodology must be identified and approved by H+H prior to study implementation.

SECTION 30. RESEARCH RELATED INJURIES: TREATMENT AND REIMBURSEMENT

30.1 Policy

30.1.1 General.

Federal regulations require that, for Human Subjects Research involving more than minimal risk, prospective Research Project subjects be provided with an explanation as to whether any medical treatments will be provided if an injury occurs and if so, what they consist of, or where further information may be obtained.¹⁶⁷

This Section defines what treatment H+H will provide to Human Subjects as a result of a Research Related Injury, and defines H+H's requirements for Sponsors of Research regarding Research Related Injuries.

30.1.2 Treatment of Research Related Injuries.

If a Human Subject suffers a Research Related Injury as a direct result of Research participation, it is the policy of H+H to provide emergency medical treatment to the Human Subject. The Human Subject may be responsible for any permissible deductibles or co-pays as required by his/her insurance carrier.

30.1.3 Reimbursement for Research Related Injuries.

(a) *For Research Projects Funded by a Sponsor.* The Office of Research Administration will review the applicable Research agreement to determine H+H's obligations under this Section. H+H's obligations under this Section will be secondary to the Sponsor's obligations under any clinical trial or other Research agreement between Sponsor and Grantee.

(b) *For All Research Projects.* The Informed Consent shall direct Human Subjects suffering a Research Related Injury to report the injury to the Principal Investigator as promptly as possible.

30.1.4 Limitation of Obligation.

(a) *H+H Obligations.* The obligation of H+H undertaken in this Section shall be limited to those injuries for which notification and determination have been made in accordance with the procedures described below.

(b) *Consequential and Special Damages.* Except for claims arising from demonstrated negligence on the part of H+H, H+H's current policy does not provide for compensation of a Human Subject suffering a Research Related Injury through payments for lost wages, cost of pain and suffering, or additional expenses beyond those of medical care. Any compensation claims received for reimbursement of costs and expenses beyond the provision of medical care must be handled on a case-by-case basis in consultation with the Office of Legal Affairs.

30.2 Definitions.

For purposes of this Section 30, the following definitions shall apply.

“Research Related Injury” means an injury or illness which occurs to a Human Subject as a result of participating in a Research Project.

30.3 Procedures.

30.3.1 Initial Notification and Preliminary Review. H+H's obligations regarding treatment of Research Related Injuries shall be subject to the following conditions:

(a) Written notification of any injury believed by the Human Subject to be a Research Related Injury must be documented by the applicable Principal Investigator within a reasonable time after discovery.

(b) The Principal Investigator of the Research Project is responsible for (i) notifying the Facility medical director and FRRC about the above notification by the Human Subject, and (ii) evaluating Human Subjects who claim to have a Research Related Injury and making a preliminary determination as to whether the injury is a) a Research Related Injury, or b) an Unanticipated Problem Involving Risks to Human Subjects or Others as defined in Section 25.1.2. In making this determination, the Principal Investigator should review the Research Protocol, any consent forms signed by the Human Subject, investigator brochure or drug labeling and pertinent medical literature. The Principal Investigator shall also consult with the IRB as appropriate.

(i) Upon determining that a Human Subject may have suffered a Research Related Injury, the Principal Investigator must report the claimed Research Related Injury to the Facility's medical director, copying

the Office of Research Administration, the IRB and the Principal Investigator's respective FRRC as promptly as possible. Only injuries that the Principal Investigator determines meets the definition of Research Related Injury should be reported in this manner.

- (ii) Research Related Injuries must also be reported to the IRB.

30.3.2 Determination.

(a) The Principal Investigator will promptly notify the IRB, Office of Research Administration and FRRC Chair of all Research Related Injuries. The Principal Investigator will determine in collaboration with the FRRC Chair and IRB whether a Research Related Injury is an Unanticipated Problem involving risks to Human Subjects or Others, as defined in Section 25.1.2. The FRRC will advise the applicable Facility's finance department to flag charges while internal assessments are underway.

(b) The Principal Investigator together with the IRB will be responsible for making the final determination of whether a Research Related Injury covered by this Section 30 has occurred and resulted directly from the Human Subject's participation in the Research Project.

(c) If the Principal Investigator and IRB conclude that a Research Related Injury has occurred, and such injury is not eligible for reimbursement by a Sponsor, the charges will be removed from the Human Subject's bill by the Facility's finance department. Any required refunds or adjustments will be made for charges already paid for by the Human Subject or his or her insurance plan.

SECTION 31. RESEARCH COSTS

31.1 Policy

H+H will work with researchers and Affiliates to encourage Research throughout the H+H system. Where Research for which an Affiliate is the Grantee is conducted at an H+H Facility, however, H+H cannot financially absorb all of the costs for the use of its Facilities to carry out such Affiliate research. Therefore, Facility resources will not be committed and Research will not be approved by H+H (through the approval process outlined in Section 4 and Section 12 of these Policies and Procedures) to be conducted at a Facility by a Principal Investigator or any person unless H+H and the Facility have reviewed and approved all costs that may be incurred by the accomplishment of such Research, and the Affiliate and H+H have agreed in writing as to how such costs will be reimbursed to H+H.

31.2 Definitions

For purposes of this Section 31, the following definitions shall apply.

“Research Project Costs” means the amount due to H+H from an Affiliate when such Affiliate is the Grantee with respect to a specific Research Project and the Research is conducted at an H+H Facility, such amount being calculated under an agreement between H+H and the Affiliate that includes terms for reimbursement of such costs.

31.3 Procedures

31.3.1 Preparation of Budget for Research Project. Where there is an application for external funding for Research to be conducted at a Facility, the finance department of the Facility will assist the Principal Investigator in the preparation of a budget for the Research Project that sets forth those activities that are standard of care and those that are strictly Research related. The Facility will provide relevant budget information to the Principal Investigator in a timely manner. A copy of relevant financial sections shall be provided to the Facility and to H+H as part of the Research approval process described in Section 4 of these Policies and Procedures. The Facility will obtain all salary and related personnel services information from the Affiliate.

31.3.2 Items To Be Included In Proposed Budget.

(a) The procedure for preparing a proposed budget should be considered with any affiliation agreement and/or research agreement in place between an Affiliate and H+H.

(b) If a research agreement exists between an Affiliate and H+H, the proposed budget must give sufficient financial information to allow the parties to comply with the compensation requirements of such agreement. Such proposed budget must include a breakdown by billable and funded services, providing enough information to support to supply a complete picture of the actual cost and benefit of the project.

(c) If a research agreement does not exist between the Affiliate and H+H, and the applicable affiliation agreement does not contain conflicting provisions, the following will apply:

(i) *Direct Costs.* Regardless of funding source, the proposed budget must list anticipated total direct costs, including, but not limited to, any applicable research fees, any facility resource usage fees (e.g., salary, fringe and other than personal services “OTPS”) and all indirect costs.

(ii) *Indirect Costs.* With respect to indirect costs, if H+H is the Grantee, then, for all Federal grants, the proposed budget must utilize the indirect cost rate previously negotiated with the Federal government. If the source of funding is other than the Federal government, the proposed budget must utilize the indirect cost rate negotiated with the funding source and approved by the Office of Research Administration. If an Affiliate is a subcontractor to H+H then the proposed budget should state the amounts to be paid to the Affiliate pursuant to the agreement negotiated with the Affiliate and approved by the Office of Legal Affairs.

(d) *Affiliate Payments.* Where an Affiliate is the Grantee, the proposed budget must include the amounts, including the indirect overhead rate, negotiated with the Affiliate and payable to H+H as subcontractor.

(e) *H+H Direct Costs.* It is the expectation of H+H that H+H employees, H+H agents, or H+H subcontractors, as designated by H+H, contribute directly to the science of Research Projects conducted at a Facility and be recognized as Principal Investigators or Sub-investigators through the awarding subcontracts and that H+H employees, agents, or subcontractors will be utilized to participate in such studies.

31.3.3 H+H Costs.

(a) Where the Affiliate is the Grantee with respect to a Research Project, the Facility will invoice such Affiliate for the Research Project Costs in accordance with the terms of the applicable agreement H+H has with such Affiliate according to the terms established in such agreement.

(b) On a case by case basis, where permitted by law, the Facility's Executive Director may waive all or a portion of the Research Project Costs where such Executive Director deems it appropriate. Before such a waiver may be given, however, all Research related costs must be identified and documented by the Facility and given to the Executive Director.

31.3.4 Affiliate Costs. Where H+H is the Grantee and where an Affiliate incurs costs due to Research conducted at a Facility, H+H will reimburse that Affiliate for such costs in accordance with any applicable provisions of an agreement with a Sponsor or Grantor and H+H's policies, procedures and applicable law.

31.3.5 Purchase of Budgeted Items. If the purchase of any items, including but not limited to equipment, are specifically budgeted for as part of an approved Research Project and required by the Contract or Grant, such items should be purchased following the guidelines outlined in H+H Operating Procedure 100-5: Procurement Methods, Required Approvals and Reporting.

31.3.6 Travel Related to Research Project.

(a) The requirements of H+H Operating Procedure 10-10: Official Travel and Miscellaneous Business Expense will not apply to travel and travel-related expenses which are:

(i) Required by a Grant or Contract of an approved Research Project, and

(ii) Are specifically included in the budget for the subject Research Project.

- (b) If no specifications or restrictions are delineated and budgeted by the Grant or Contract, however, H+H Operating Procedure 10-10: Official Travel and Miscellaneous Business Expense shall apply.

SECTION 32. RESEARCH TIME AND EFFORT REPORTING

(Please see H+H Time and Effort Policy and Procedure Number 40-61).

SECTION 33. BILLING COMPLIANCE

33.1 Policy

33.1.1 General. H+H requires that all clinical services, items or tests billed to Grantors, Sponsors, Human Subjects, Medicare, Medicaid, or other third party payors be:

- (a) Consistent with applicable billing rules of the third party payor being billed,
- (b) Consistent with any Grant provisions or obligation under a Contract entered into by H+H,
- (c) Represented consistently across all award-related documents, including the Research Protocol, Grant, Contract, budget and Informed Consent, and
- (d) Consistent with H+H procedures that establish safeguards to prevent billing mistakes.

33.1.2 Importance of Proper Billing. Billing for clinical research services provided to Human Subjects enrolled in Research Projects is complex because it often involves more than one entity that is responsible for costs incurred by the study. The complexity of the rules require that H+H work collaboratively with the Facilities and Affiliates to ensure that costs associated with a Grant or Contract are billed in compliance with relevant laws and regulations.

33.1.3 Possible denial of claims and direct liability of Principal Investigator. Should the Centers for Medicare and Medicaid Services find that it was incorrectly billed for items not meeting the qualifying criteria in order to gain Medicare coverage of Routine Costs of a Clinical Trial, Medicare coverage of such routine costs would be denied to H+H. Moreover, H+H could be held liable for such costs and investigations of H+H and the trial's Principal Investigator may also be open to more scrutiny by CMS.¹⁶⁸

33.1.4 Laws, Regulations and Guidance that Affect Billing Compliance.

- (a) *45 C.F.R. Part 75.* These principles identify the general accounting rules for hospitals and define those costs that are allowable to Research funded by

an agency of the Federal government. Any cost being charged to a Federal funding agency must satisfy the following criteria:

- (i) The cost must be allowable as defined by Title 45 C.F.R. Part 75, and/or by the terms of the particular Grant.¹⁶⁹
- (ii) The cost must be allocable (i.e., the project that paid the expense must benefit from it).¹⁷⁰
- (iii) The expense must be reasonable (i.e., the cost reflects what a “prudent person” might pay).¹⁷¹
- (iv) The expense must be consistent with costs charged in similar circumstances to other Research Projects.

If costs are not allowable, reasonable and consistent, then they may not be charged to a Research Project.

(b) *NIH Grants Policy Statement, October 2017.* For Federally funded clinical trials, H+H is subject to the regulations located in the NIH Grants Policy Statement listed under the heading Routine Patient Care Costs.¹⁷² Research patients may receive Routine Services as inpatients, or Ancillary Services as either inpatient or outpatient subjects/volunteers. H+H is required under NIH policy to negotiate a research patient care rate agreement with the cognizant Division of Cost Allocation (DCA) office of the United States Department of Health and Human Services.¹⁷³ These rates must be used in requests and/or claims for reimbursement of Routine Patient Care Costs for all Federally funded clinical trials. Failure to negotiate a research patient care rate with DCA when required may result in the disallowance of all Routine Patient Care Costs charged to a Grant. H+H’s current rate agreement will be posted on the Research Administration Intranet website.

(c) *Centers for Medicare and Medicaid Services National Coverage Decision for Routine Costs of a Clinical Trial, July 9, 2007 (“NCD”).* Under the NCD, coverage of Routine Costs of a Clinical Trial is allowed only during a qualified clinical trial. Medicare and other third party insurers will not cover routine costs that are paid for by the Grantor/Sponsor, promised free in the Informed Consent document, not ordinarily covered by Medicare or solely to determine trial eligibility or for data collection or analysis.¹⁷⁴

(d) *Federal and State Billing Manuals.*

(i) Medicare Carriers Manual. Program instructions are day-to-day operating instructions, policies, and procedures based on statutes and regulations, guidelines, models, and directives. They are used by CMS program components, contractors, and state survey agencies to administer CMS programs. For many others, they are a good source of technical and professional information about the Medicare and Medicaid programs.

(ii) Medicaid Manual. The NYSDOH provides rules for documentation, coding and billing for reimbursement under the New York State Medicaid program.

(e) *Other Federal Laws*. Other Federal statutes and regulations, such as the Anti-Kickback Statute, Stark Laws, Deficit Reduction Act of 2005, Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Programs (codified at 2 CFR Part 200) and the Federal False Claims Act also govern the billing and management of clinical trials and Federal grants and contracts.

33.2 Definitions

For purposes of this Section 33, the following definitions shall apply.

“Affiliate Providers” means Physicians, residents and other professional staff employed by an Affiliate and possessing medical staff privileges at a Facility.

“Ancillary Services” means those special services for which charges are customarily made in addition to Routine Services (e.g., x-ray, operating room, laboratory, pharmacy, blood bank, and pathology).

“Contract” means, in general terms, financial assistance given to H+H by a Sponsor for a specific purpose to support instruction, research, or health or other public service.

“Coverage Analysis” means the coverage analysis as described in Section 33.3.2(a).

“Facility Executive Director” means the person then serving as the executive director of a Facility.

“Facility Financial Analyst” or **“FFA”** means an individual who carries out the activities described in Section 33.3.2 and who is designated by the Facility Executive Director. The FFA should be an individual with experience and knowledge with respect to research, costs and budgets, such as the FRCC director or other individual as determined by the Facility Executive Director.

“Facility Personnel” means all individuals who serve at a Facility as patient service representatives, billers, coders, clinic administrators and service providers.

“Fixed Price Award” means a Grant or Contract between: (1) a Grantee or a Sponsor or, a Grantee and a Grantor; (2) in which the Research Project is negotiated at a preset amount, regardless of actual costs.

“Key Staff” means the Research Team and Affiliate Providers. Key Staff also include Facility Personnel and any other individual employed at H+H and/or a Facility who is responsible for any aspect of billing for services or items provided by H+H during the course of Research on behalf of H+H funded by a third party.

“Routine Costs of a Clinical Trial” means the costs of a clinical trial which include all items and services that are otherwise generally available to Medicare beneficiaries and services that are

provided in either the experimental or the control arms of a clinical trial. Routine Costs of a Clinical Trial include:

- Items or services that are typically provided absent a clinical trial (e.g., conventional care);
- Items or services required solely for the provision of the investigational item or service (e.g., administration of a non-covered chemotherapeutic agent), the clinically appropriate monitoring of the effects of the item or service, or the prevention of complications; and
- Items or services needed for reasonable and necessary care arising from the provision of an investigational item or service--in particular, for the diagnosis or treatment of complications.

Routine Costs of a Clinical Trial do not include:

- The investigational item or service itself unless otherwise covered outside of the clinical trial or specified in the contract;
- Items and services provided solely to satisfy data collection and analysis needs and that are not used in the direct clinical management of the patient (e.g., monthly CT scans for a condition usually requiring only a single scan); and
- Items and services customarily provided by the Grantor or Sponsor free of charge for any enrollee in the trial.

“Routine Patient Care Costs” means the costs of Routine Services and Ancillary Services provided by H+H to individuals participating in Research Studies that are reimbursed by a specific Research Project. Routine Patient Care Costs do not include: (1) the otherwise allowable items of personal expense reimbursement, such as patient travel or subsistence, consulting physician fees, or any other direct payments related to all classes of individuals, including inpatients, outpatients, subjects, volunteers, and donors, (2) costs of ancillary tests performed in facilities outside the hospital on a fee-for-service basis (e.g., in an independent, privately owned laboratory) or laboratory tests performed at a medical school/university not associated with a hospital routine or ancillary service, (3) recruitment or retention fees or (4) the data management or statistical analysis of clinical research results.¹⁷⁵

“Routine Services” means regular room services, minor medical and surgical supplies, and the use of equipment and facilities, for which a separate charge is not customarily made.

33.3 Procedure

33.3.1 Roles and Responsibilities.

(a) *H+H Facilities.*

(i) Will implement mechanisms that enable billing of Research-related encounters to the appropriate Grants or Contracts.

(b) *Principal Investigator.*

(i) Together with the Sponsor/Grantor is responsible for the terms and conditions of the Research Project and its related budget.

(ii) Must understand and comply with all rules for billing Medicare, Medicaid and third party insurers for services provided in the context of clinical research.

(iii) Identify, with the assistance of the Facility Financial Analyst, which services are billable to a third party payor, including Medicare or Medicaid and which services will be covered by the Grant or Contract.

(iv) If hospital ancillary services are utilized, Principal Investigator must send a copy of the final protocol and draft budget to the Facility Financial Analyst for review and approval of fees prior to submission to the Sponsor or Grantor.

(c) *Facility Financial Analyst (FFA).*

(i) Work with the Principal Investigator and study staff to review and approve rates/fees associated with hospital ancillary services.

(ii) Assist the Principal Investigator and his/her study team to create a detailed per subject Coverage Analysis of the protocol, if needed, regardless of funding source.

(iii) Review the amounts billable to third-party payors and amounts that may be applied against Contracts or Grants as generated by the system designated by H+H.

(iv) Review amounts payable to patients, overseeing both cash and non-cash distributions to patients and reconciling such distributions.

(v) Make certain that services for patients enrolled in Research Projects are billed and recorded in accordance with the assessments previously determined in the executed Contract/Grant and budget.

(vi) On a monthly basis, invoice Grantors for studies utilizing hospital services based on FFA review of the billable amounts generated by the system designated by H+H.

(vii) On a quarterly basis, invoice Sponsors for milestone payments or provide documentation and data as required in the relevant Contract or approved Research Protocol.

(viii) Communicate to the Facility Finance Office what amounts may be billed to third-party payors.

(ix) Correct any research billing discrepancies (e.g., unbilled services) or errors on patient accounts which are identified by or reported to the FFA.

(d) *Office of Research Administration.*

(i) Provide the FFA with copies of proposed Contracts/Grants, and template budgets that will be utilizing hospital services.

(ii) Negotiates all Contracts/Grants and budgets.

(e) *Study Coordinators.* Tracking patients enrolled in studies, scheduling appointments and maintaining records in accordance with the instructions of the Principal Investigator or policies of the contracting organization.

(f) *Ancillary Department.* Establish procedures to ensure ancillary and professional services are billed appropriately to the Contract/Grant, the patient or to the appropriate third party payor, as previously determined in the executed Contract/Grant and budget.

(g) *Facility Finance Office.* Establish procedures to ensure that funds received through a Contract/Grant are segregated and used appropriately in accordance with the terms and conditions of the Contract/Grant, and for facilitating appropriate cost transfers.

33.3.2 Billing Procedures

(a) If the Research Protocol and/or the Contract/Grant mentions payment for treatment, or items of services that would be a Routine Cost of Clinical Trial or a Routine Patient Care Cost and such items of service or treatment could be billable to a third party payor, the Principal Investigator, with the assistance of the Facility Financial Analyst, shall perform a Coverage Analysis. . The Coverage Analysis involves determining the underlying eligibility of the study for Medicare and other third party coverage and review of the clinical events specified in the Research Protocol to determine which items can be reimbursed by Medicare and other third party payors. For Federally funded Research, or trials funded by not-for-profit organizations, the requirements of NIH Grants Policy Statement must be

followed with regard to Routine Patient Care Costs. Where Medicare is a third-party payor the Medicare National Coverage determinations Manual 310.1 (entitled Routine Costs in Clinical Trials) as modified by Medicare Coverage Decision Memorandum for the Clinical Trial Policy dated July 9, 2007, must be followed with respect to reimbursement for Routine Costs of a Clinical Trial.

(b) Based on the Coverage Analysis and the draft contract with the Grantor or Sponsor the Facility Financial Analyst will create a draft budget which will be reviewed and approved by the Principal Investigator. The Facility Financial Analyst will transmit this draft budget to the Office of Research Administration who will utilize this budget in its negotiations with the Sponsor/Grantor. If the Grantor or Sponsor has offered to pay for all visits, treatments and services, a Coverage Analysis should still be completed in the event unanticipated routine costs arise.

(c) The Principal Investigator will register patients, with the assistance of the Study Coordinators, and input patient treatment information with appropriate research and treatment codes, as stipulated by the research agreement, into the clinical and billing systems designated by H+H. The Principal Investigator will use the non-billable research code designated by the Facility or any other mechanism designated by the Facility to ensure that the billing system of that Facility does not generate a bill for such research service(s).

(d) A system designated by H+H generates reports of the amounts billable to third-party payors. Such reports shall be reviewed by the Facility Financial Analyst to confirm that the proper party is being billed for the appropriate items, taking into account the terms of the applicable Contract/Grant and budget to verify what the Sponsor/Grantor will cover, as well as the requirements regarding Routine Patient Care Costs¹⁷⁶ and regarding Routine Costs in Clinical Trials.¹⁷⁷ As appropriate, the FFA will work together with the Principal Investigator to confirm the accuracy of the amounts proposed to be billed to third-party payors or against the studies.

(e) The Facility Financial Analyst communicates to the Facility Finance office what amounts may be billed to third-party payors. The Facility Financial Analyst will work with the Facility Finance Office to ensure that the funding source for each Research Project is identified individually, and that the funds for each Research Project are used only for their intended purpose in accordance with the terms of the Grant or Contract and applicable law and regulation.¹⁷⁸

(f) On a regular, typically monthly, basis or as defined in the Grant, the FFA invoices Grantors for studies utilizing hospital services based on FFA review of the billable amounts and in accordance with the terms of the Grant.

(g) On a regular, typically quarterly, basis or as defined in the Contract, FFA invoices Sponsors for milestone payments or provide documentation and data as required in the relevant Contract or approved Research Protocol.

33.3.3 Reconciliation of Payments. The Facility Financial Analyst should reconcile all payments to ensure that all payments due to H+H have been received. Once the study is closed, final payment has been received, and all outstanding obligations have been paid, FFAs should contact the Office of Research Administration to close the account.

33.3.4 Education and Training. Office of Research Administration at Central Office and Facility Executive Director shall be responsible for ensuring that H+H policies concerning billing compliance are disseminated and understood.

33.3.5 Sanctions.

(a) Non-compliance with this Section 33 shall include, but is not limited to, the submission of incomplete, erroneous, or misleading billing. Non-compliance with this Section 33 will result in H+H taking any action required to comply with Federal and State requirements.

(b) Individuals who engage in such non-compliance shall also be disciplined in accordance with H+H's Employee Disciplinary Policy and/or Medical Staff By-Laws.

(c) Non-compliance with this Section 33 may also result in penalties levied against the departments, divisions, Affiliates and/or H+H.

SECTION 34. RESIDUAL BALANCE ON FIXED PRICE AWARDS AND SPONSOR CONTRACTS

34.1 Policy

Certain awards are negotiated on a fixed price basis. On occasion, a Residual Balance will remain after all costs and revenue have been properly accounted for with respect to a Research Project. While Residual Balances on non-government awards are not restricted, the regular occurrence of large Residual Balances may indicate problems with accounting and budget estimation processes, and could expose H+H, the Facility, the Principal Investigator and other researchers, and the IRB to conflict of interest, anti-kickback and other liability.

The disposition of a Residual Balance is generally determined in accordance with the terms of the award. Grantors and Sponsors may require Residual Balances to be returned to them upon completion of the Research Project. If the award is silent as to how a Residual Balance should be handled at the close or termination of the Research Project, Residual Balances will be handled in accordance with the procedures set forth below.

34.2 Definitions

For purposes of this Section 34 the following definitions shall apply.

“Current Budget Period” shall mean the fiscal time period designated for a given award pursuant to the terms of the award. The Current Budget Period is commonly a year, but may be less than a year or consist of multiple years, depending on the method of funding of the Grantor or Sponsor.

“Residual Balance” means any unobligated, unspent balance remaining from the funds received from a Grantor or Sponsor at the conclusion of the Research Project.

34.3 Procedure

34.3.1 Quarterly Distributions of Anticipated Overage.

(a) Prior to the commencement of the Current Budget Period of a Fixed Price Grant, the Principal Investigator, Facility Research Office and Facility Finance Office will discuss and agree upon any expected overage (the “Anticipated Overage Amount”) for the Current Budget Period. The Anticipated Overage Amount will be divided by the number of months in the Current Budget Period and transferred quarterly into a designated account at the Facility at which such Research Project is conducted for the Department and Principal Investigator that conducted the Research Project (the “Designated Account”).

(b) Within ten (10) days of the end of the Current Budget Period, the Finance Office will reconcile the actual Residual Balance against the Anticipated Overage Amount distributed to the Designated Account. If the Anticipated Overage Amount is different than the actual Residual Balance, the Finance Office shall withdraw or transfer monies from or to the relevant account to reconcile such difference.

(c) Residual funds will be transferred under this Section without adjustment if the award was negotiated with the Sponsor or Grantor at the full indirect cost rates, as approved by H+H’s cognizant agency. If not, before any transfer to the Designated Account as described above, the residual funds will be adjusted to reflect the full recovery of H+H’s indirect costs.

34.3.2 Researcher Certified Statement. If there is a Residual Balance at the end of the Current Budget Period of a Fixed Price Grant, the Principal Investigator, Department Chair or designee will certify the following and submit such certified statement to the Office of Research Administration with a copy to the Facility Finance Office and the Facility Research Office:

(a) All income has been received for the Research Project for the Current Budget Period;

(b) All tasks required to be completed for the Research Project for the Current Budget Period have been completed;

(c) All reports or other deliverables for the Current Budget Period have been provided to the Grantor or Sponsor;

(d) All expenses charged by the Principal Investigator for the Current Budget Period have been properly charged to the Research Project; and

(e) The award does not require return of unexpended funds for Current Budget Period.

34.3.3 Facility Finance Office Certified Statement. After performing the reconciliation pursuant to Section 34.3.1(b), above, the Facility Finance Office shall certify that the reconciliation was completed and that all the expenses for the Current Budget Period have been properly charged to the relevant Research Project. The Facility Finance Office shall transmit such certified statement to the Office of Research Administration with a copy to the Facility Research Office and the relevant Department Chair.

34.3.4 Office of Research Administration Review and Approval.

(a) The Office of Research Administration may, within ten (10) days of its receipt of both certified statements listed above, request further information as to the reason for the Residual Balance, including but not limited to, if the Residual Balance is in excess of 20% of the contract amount for the applicable Current Budget Period. The Office of Research Administration may delegate this review to the relevant Facility Research Office.

(b) The Office of Research Administration must complete its review within thirty (30) days of its receipt of both certified statements listed above. In the case where the Office of Research Administration disagrees with the request, it must communicate to the persons submitting such certified statements any reason why it believes the transfer of the funds should be reversed. Prior to a decision to reverse the request, the Office of Research Administration must discuss this decision with the Principal Investigator to ensure a full understanding of the project and finances. If rejected, then the Office of Research Administration will meet with the Facility Finance Office, the Facility Research Office and the submitting Principal Investigator, Department Chair or designee, to determine the appropriate actions to be taken with respect to the funds. If, after the thirty day period, the Office of Research Administration makes no such communication, the transfer into the Designated Account as certified by the Facility Finance Office is deemed approved.

34.3.5 Residual Balance on Sponsor Contracts. Any Residual Balance remaining on a Sponsor Contract shall be returned to the Sponsor, unless otherwise specified in the Contract or otherwise agreed to by the Sponsor.

34.3.6 Uses of the Funds in Account for Research Project Residual Funds.

(a) The monies in the Designated Account are institutional funds. The Principal Investigator or Department Chair may utilize the funds in the Designated Account in any manner he or she deems appropriate only for the advancement of Research at H+H, following the procedures outlined in Section 34.3.6(d) below.

(b) Notwithstanding the above, these funds can only be used for other-than-personal-services (OTPS) expenditures, except as provided in Section 34.3.6(c), below, and may not be utilized for any of the following:

(i) Salary, bonuses or salary raises or any other compensation to any researcher whether employed by H+H, employed by an Affiliate or working as an independent contractor;

(ii) The purchase or lease of any items for substantially personal use (e.g., a car, a television, a boat, etc.);

(iii) Activities or events for substantially personal reasons (e.g., family vacation, travel, parties, entertaining etc.);

(iv) Expenditures that otherwise may be reimbursable to a Principal Investigator or Department as continuing medical education expenditures, or funding which is otherwise the direct obligation of an Affiliate of H+H or a Grantor or Sponsor for research activities, postgraduate training program sponsor or medical school;

(v) No reimbursement will be made from the Designated Account for OTPS items for which H+H has reimbursed an Affiliate pursuant to an agreement with such Affiliate.

(c) For clarity, subject to Section 34.3.8, monies from the Designated Account may be used to pay for personal services that are administrative in nature (e.g., data entry, processing and shipping samples, etc.) that directly advance Research at H+H.

(d) Principal Investigator or Department Chair shall submit receipts and other evidence of completed payment as H+H should request, to the relevant Facility Finance Office, describing the reason for such expenditures. If the reason for the expenditure is found to advance Research at H+H and is not a prohibited expenditure listed in Section 34.3.6(b) above, the monies shall be released to the Principal Investigator or the Department in a timely manner. Alternatively, the Principal Investigator or Department Chair may, at their option, first submit a request to the Facility Finance Office for funds in anticipation of expenditure to be paid from the Designated Account, stating the reason for the anticipated expenditure and providing any further documentation required by the Facility Finance Office to review the request. If the request is granted, the Facility Finance Office shall pay the requested expense directly to the third-party(ies), as described in submitted request. Periodically, but not less frequently than semi-annually, the Facility Finance Office will engage in a reconciliation, ensuring that no monies have been paid out of the Designated Account for items that were also paid to an Affiliate under an agreement with such Affiliate. If such double payment is found to have occurred, H+H may offset such amount by any amounts in the Designated Account.

34.3.7 In the event that a Principal Investigator resigns, retires, or is no longer affiliated with H+H for any reason, the amount in the Designated Account associated with that Principal Investigator may not be paid to such Principal Investigator and may be expended only by the relevant Department, or may be reassigned for use by another Principal Investigator by the chair of such Department.

34.3.8 Where an agreement with an Affiliate requires the funding of personal services positions with Residual Balances, the Anticipated Overage Amount referenced in Section 34.3.1 above, will be first reduced by such amounts payable to the Affiliate for such positions before any transfer to the Designated Account may occur. Notwithstanding Section 34.3.6(c) monies in the Designated Account may not be used to pay for any personal services, whether or not administrative in nature, if such personal services position is described in and compensated through an agreement with an Affiliate.

EXHIBIT 1

BELMONT REPORT

Federal Register

Part IV

**Department of
Health, Education,
and Welfare**

Office of the Secretary

**Protection of Human Subjects; Notice of
Report for Public Comment**

**DEPARTMENT OF HEALTH,
EDUCATION, AND WELFARE**

Office of the Secretary

Protection of Human Subjects;

**Belmont Report: Ethical
Principles and Guidelines for the
Protection of Human Subjects of
Research, Report Of the National
Commission for the Protection of
Human Subjects of Biomedical
and Behavioral Research**

AGENCY: Department of Health,
Education, and Welfare.

ACTION: Notice of Report for
Public Comment.

SUMMARY: On July 12, 1974, the National Research Act (Pub. L. 93-348) was signed into law, thereby creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. One of the charges to the Commission was to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles. In carrying out the above, the Commission was directed to consider: (i) the boundaries between biomedical and behavioral research and the accepted and routine practice of medicine, (ii) the role of assessment of risk-benefit criteria in the determination of the appropriateness of research involving human subjects, (iii) appropriate guidelines for the selection of human subjects for participation in such research, and (iv) the nature and definition of Informed Consent in various research settings.

The Belmont Report attempts to summarize the basic ethical principles identified by the Commission in the course of its deliberations. It is the outgrowth of

an intensive four-day period of discussions that were held in February 1976 at the Smithsonian Institution's Belmont Conference Center supplemented by the monthly deliberations of the Commission that were held over a period of nearly four years. It is a statement of basic ethical principles and guidelines that should assist in resolving the ethical problems that surround the conduct of research with human subjects. By publishing the Report in the Federal Register, and providing reprints upon request, the Secretary intends that it may be made readily available to scientists, members of Institutional Review Boards, and Federal employees. The two-volume Appendix, containing the lengthy reports of experts and specialists who assisted the Commission in fulfilling this part of its charge, is available as DHEW Publication No. (OS) 78-0013 and No. (OS) 78-0014, for sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

Unlike most other reports of the Commission, the Belmont Report does not make specific recommendations for administrative action by the Secretary of Health, Education, and Welfare. Rather, the Commission recommended that the Belmont Report be adopted in its entirety, as a statement of the Department's policy. The Department requests public comment on this recommendation.

DATES: The Secretary invites comment on the Belmont Report. The comment period will close July 17, 1979.

ADDRESSES: Please send comments or requests for additional information to: F. William Dommel, Jr., J.D., Assistant Director for Regulations, Office for Protection from Research Risks, National Institutes of Health, 5333 Westbard Avenue, Room 303, Bethesda, Maryland 20205,

telephone: 301-496- 7005 where all comments received will be available for inspection weekdays (Federal holidays excepted) between the hours of 9 a.m. and 4:30 p.m.

DATED: March 30, 1979.

Charles Miller,
Acting Assistant Secretary for Health.

Approved April 12, 1979.

Joseph A. Califano Jr.,
Secretary.

National Commission for the
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Biomedical and Behavioral
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**Belmont Report
Ethical Principles and Guidelines
for Research Involving Human
Subjects**

Scientific research has produced
substantial social benefits. It has
also posed some troubling ethical
questions. Public attention was
drawn to these questions by
reported abuses of human subjects
in biomedical experiments,
especially during the Second World
War. During the Nuremberg War
Crime Trials, the Nuremberg Code
was drafted as a set of standards for
judging physicians and scientists
who had conducted biomedical
experiments on concentration camp
prisoners. This code became the
prototype of many later codes*

intended to assure that research
*Since 1945, various codes for the
proper and responsible conduct of

human experimentation in medical
research have been adopted by
different organizations. The best
known of these codes are the
Nuremberg Code of 1947, the
Helsinki

Declaration of 1964 (revised in
1975), and the 1971

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involving human subjects would
carried out in an ethical manner.
The codes consist of rules, some
general, others specific, that guide
the investigators or the reviewers of
research in their work. Such rules
often are inadequate to cover
complex situations: at times they
come into conflict, and they are
frequently difficult to interpret or
apply. Broader ethical principles
will provide a basis on which
specific rules may be formulated,
criticized and interpreted.

Three principles, or general
prescriptive judgements, that are
relevant to research involving
human subjects are identified in
this statement. Other principles
may also be relevant. These three
are comprehensive, however, and
are stated at a level of
generalization that should assist
scientists, subjects, reviewers and
interested citizens to understand the
ethical issues inherent in research
involving human subjects. These
principles cannot always be applied
so as to resolve beyond dispute
particular ethical problems. The
objective is to provide an analytical
framework that will guide the
resolution of ethical problems
arising from research involving
human subjects.

This statement consists of a
distinction between research and
practice, a discussion of the three
basic ethical principles, and
remarks about the application of
these principles.

**A. Boundaries Between Practice
and Research**

It is important to distinguish
between biomedical and behavioral
research, on the one hand, and the
practice of accepted therapy on the
other, in order to know what
activities ought to
undergo review for the protection
of human subjects of research. The
distinction between research and
practice is blurred partly because
both often occur together (as in
research designed to evaluate a
therapy) and partly because notable
departures from standard practice
are often called "experimental"
when the terms "experimental" and
"research" are not carefully
defined.

For the most part, the term
"practice" refers to interventions
that are designed solely to enhance
the well-being of an individual
patient or client and that have a
reasonable expectation of success.
The purpose of medical or
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Guidelines (codified into Federal
Regulations in 1974) issued by the
U.S. Department of Health,
Education, and Welfare. Codes for
the conduct of social and
behavioral research have also been
adopted, the best known being that
of the American Psychological
Association, published in 1973.
behavioral practice is to provide
diagnosis, preventive treatment or
therapy to particular individuals.*
By contrast, the term "research"
designates an activity designed to
test an hypothesis, permit
conclusions to be drawn, and
thereby to develop or contribute to
generalizable knowledge
(expressed, for example, in
theories, principles, and statements
of relationships). Research is
usually described in a formal
protocol that sets forth an objective
and a set of procedures designed to
reach that objective.

When a clinician departs in a
significant way from standard or
accepted practice, the innovation
does not, in and of itself, constitute
research. The fact that a procedure

is "experimental," in the sense of new, untested or different, does not, automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.*

Research and practice may be carried on together when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

*Although practice usually involves interventions designed solely to enhance the well-being of a particular individual, interventions are sometimes applied to one individual for the enhancement of the well-being of another (e.g., blood donation, skin grafts, organ transplants) or an intervention may have the dual purpose of enhancing the well-being of a particular individual, and, at the same time, providing some benefit to others (e.g., vaccination, which protects both the person who is vaccinated and society generally). The fact that some forms of practice have elements other than immediate benefit to the individual receiving an intervention, however, should not confuse the general distinction between research and practice. Even when a procedure applied in practice may benefit some other person, it remains an intervention designed to enhance the well-being of a particular individual or groups of individuals; thus, it is practice

and need not be reviewed as research.

* Because the problems related to social experimentation may differ substantially from those of biomedical and behavioral research, the Commission specifically declines to make any policy determination regarding such research at this time. Rather, the Commission believes that the problem ought to be addressed by one of its successor bodies.

B. Basic Ethical Principles

The expression "basic ethical principles" refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions. Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect for persons, beneficence and justice.

1. Respect for Persons. —Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.

An autonomous person is an individual capable of deliberation about personal goals and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons' considered opinions and choices while refraining from obstructing their actions unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that persons's considered judgments, to deny an individual

the freedom to act on those considered judgments, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

However, not every human being is capable of self-determination. The capacity for self-determination matures during an individual's life, and some individuals lose this capacity wholly or in part because of illness, mental disability, or circumstances that severely restrict liberty. Respect for the immature and the incapacitated may require protecting them as they mature or while they are incapacitated.

Some persons are in need of extensive protection, even to the point of excluding them from activities which may harm them: other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequences. The extent of protection afforded should depend upon the risk of harm and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated and will vary in different situations.

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In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly

influenced to engage in research activities for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect, itself.

2. **Beneficence.**—Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not harm and (2) maximize possible benefits and minimize possible harms.

The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard

extended it to the realm of research, saying that one should not injure one person regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment." Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

The obligations of beneficence affect both individual investigators and society at large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge and from the development of novel medical, psychotherapeutic, and social procedures.

The principle of beneficence often occupies a well-defined justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research involving children—even when individual research subjects are not direct beneficiaries. Research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices that on closer investigation turn out to be dangerous. But the role of the principle of beneficence is not always so unambiguous. A difficult ethical problem remains, for example, about research that presents more than minimal risk without immediate prospect of direct benefit to the children involved. Some have argued that such research is inadmissible, while others have pointed out that this limit would rule out much research promising great benefit to children in the future. Here again, as with all hard cases, the different claims covered by the principle of

beneficence may come into conflict and force difficult choices.

3. **Justice.**—Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property on the basis of which burdens and benefits should be distributed. These formulations are (1) to each person an equal share, (2) to each person according to individual need, (3) to each person according to individual effort, (4) to each person according to societal contribution, and (5) to each person according to merit.

Questions of justice have long been associated with social practices such as punishment, taxation and political representation. Until recently these questions have not generally been associated with scientific research. However, they are foreshadowed even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries the burdens of serving as research subjects fell

largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a particularly flagrant injustice. In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease that is by no means confined to that population. These subjects were deprived of demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available.

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

C. Applications

Applications of the general principles to the conduct of research leads to

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consideration of the following requirements: Informed Consent, risk/ benefit assessment, and the selection of subjects of research.

1. Informed Consent.— Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for Informed Consent are satisfied. While the importance of Informed Consent is unquestioned, controversy prevails over the nature and possibility of an Informed Consent. Nonetheless, there is widespread agreement that the consent process can be analyzed as containing three elements: information, comprehension and voluntariness.

Information. Most codes of research establish specific items for disclosure intended to assure that subjects are given sufficient information. These items generally include: the research procedure, their purposes, risks and anticipated benefits, alternative or invalidate the research from cases in and a statement offering the subject the opportunity to ask questions and to withdraw at any time from the research. Additional items have been proposed, including how subjects are selected, the person responsible for the research, etc.

However, a simple listing of items does not answer the question of what the standard should be for judging how much and what sort of information should be provided. One standard frequently invoked in medical practice, namely the information commonly provided by practitioners in the field or in the locale, is inadequate since research takes place precisely when a common understanding does not exist. Another standard, currently popular in malpractice law, requires the practitioner to reveal the information that reasonable persons would wish to know in

order to make a decision regarding their care. This, too, seems insufficient since the research subject, being in essence a volunteer, may wish to know considerably more about risks gratuitously undertaken than do patients who deliver themselves into the hand of a clinician for needed care. It may be that a standard of "the reasonable volunteer" should be proposed the extent and nature of information should be such that persons, knowing that the procedure is neither necessary for their care nor perhaps fully understood, can decide whether they wish to participate in the furthering of knowledge. Even when some direct benefit to them is anticipated, the subjects should understand clearly the range of risk and the voluntary nature of participation.

A special problem of consent arises where informing subjects of some pertinent aspect of the research is likely to impair the validity of the research. In many cases, it is sufficient to indicate to subjects that they are being invited to participate in research of which some features will not be revealed until the research is concluded. In all cases of research involving incomplete

disclosure, such research is justified only if it is clear that (1) incomplete disclosure is truly necessary to accomplish the goals of the research, (2) there are no undisclosed risks to subjects that are more than minimal, and (3) there is an adequate plan for debriefing subjects, when appropriate, and for dissemination of research results to them. Information about risks should never be withheld for the purpose of eliciting the cooperation of subjects, and truthful answers should always be given to direct questions about the research. Care should be taken to distinguish cases in which disclosure would destroy procedures (where therapy is

involved), which disclosure would simply inconvenience the investigator.

Comprehension. The manner and context in which information is conveyed is as important as the information itself. For example, presenting information in a disorganized and rapid fashion, allowing too little time for consideration or curtailing opportunities for questioning, all may adversely affect a subject's ability to make an informed choice. Because the subject's ability to understand is a function of intelligence, rationality, maturity and language, it is necessary to adapt the presentation of the information to the subject's capacities. Investigators are responsible for ascertaining that the subject has comprehended the information. While there is always an obligation to ascertain that the information about risk to subjects is complete and adequately comprehended, when the risks are more serious, that obligation increases. On occasion, it may be suitable to give some oral or written tests of comprehension. Special provision may need to be made when comprehension is severely limited—for example, by conditions of immaturity or mental disability. Each class of subjects that one might consider as incompetent (e.g., infants and young children, mentally disabled patients, the terminally ill and the comatose) should be considered on its own terms. Even for these persons, however, respect requires giving them the opportunity to choose to the extent they are able, whether or not to participate in research. The objections of these subjects to involvement should be honored, unless the research entails providing them a therapy unavailable elsewhere. Respect for persons also requires seeking the permission of other parties in order to protect the subjects from harm.

Such persons are thus respected both by acknowledging their own wishes and by the use of third parties to protect them from harm. The third parties chosen should be those who are most likely to understand the incompetent subject's situation and to act in that person's best interest. The person authorized to act on behalf of the subject should be given an opportunity to observe the research as it proceeds in order to be able to withdraw the subject from the research, if such action appears in the subject's best interest.

Voluntariness. An agreement to participate in research constitutes a valid consent only if voluntarily given. This element of Informed Consent requires conditions free of coercion and undue influence. Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Also, inducements that would ordinarily be acceptable may become undue influences if the subject is especially vulnerable. Unjustifiable pressures usually occur when persons in positions of authority or commanding influence—especially where possible sanctions are involved—urge a course of action for a subject. A continuum of such influencing factors exists, however, and it is impossible to state precisely where justifiable persuasion ends and undue influence begins. But undue influence would include actions such as manipulating a person's choice through the controlling influence of a close relative and threatening to withdraw health services to which an individual would otherwise be entitled.

2. Assessment of Risks and Benefits.—The assessment of risks

and benefits requires a careful arrayal of relevant data, including, in some cases, alternative ways of obtaining the benefits sought in the research. Thus, the assessment presents both an opportunity and a responsibility to gather systematic and comprehensive information about proposed research. For the investigator, it is a means to examine whether the proposed research

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is properly designed. For a review committee, it is a method for determining whether the risks that will be presented to subjects are justified. For prospective subjects, the assessment will assist the determination whether or not to participate.

The Nature and Scope of Risks and Benefits. The requirement that research be justified on the basis of a favorable risk/benefit assessment bears a close relation to the principle of beneficence, just as the moral requirement that Informed Consent be obtained is derived primarily from the principle of respect for persons. The term "risk" refers to a possibility that harm may occur. However, when expressions such as "small risk" or "high risk" are used, they usually refer (often ambiguously) both to the chance (probability) of experiencing a harm and the severity (magnitude) of the envisioned harm.

The term "benefit" is used in the research context to refer to something of positive value related to health or welfare. Unlike "risk," "benefit" is not a term that expresses probabilities. Risk is properly contrasted with harms rather than risks of harm.

Accordingly, so-called risk/benefit assessments are concerned with the probabilities and magnitudes of possible harms and anticipated benefits. Many kinds of possible harms and benefits need to be taken

into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked. Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society). Previous codes and federal regulations have required that risks to subjects be outweighed by the sum of both the anticipated benefit to the subject, if any, and the anticipated benefit to society if the form of knowledge to be gained from the research. In balancing these different elements, the risks and benefits affecting the immediate research subject will normally carry special weight. On the other hand, interest other than those of the subject may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subjects' rights have been protected. Beneficence thus requires that we protect against risk of harm to subjects and also that we be concerned about the loss of the substantial benefits that might be gained from research. The Systematic Assessment of Risks and Benefits. It is commonly said that benefits and risks must be "balanced" and shown to be "in a favorable ratio." The metaphorical character of these terms draws attention to the difficulty of making precise judgments. Only on rare occasions will quantitative techniques be available for the scrutiny of research protocols. However, the idea of systematic, nonarbitrary analysis of risks and benefits should be emulated insofar as possible. This ideal requires

those making decisions about the justifiability of research to be thorough in the accumulation and assessment of information about all aspects of the research, and to consider alternatives systematically. This procedure renders the assessment of research more rigorous and precise, while making communication between review board members and investigators less subject to misinterpretation, misinformation and conflicting judgments. Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies. Finally, assessment of the justifiability of research should reflect at least the following considerations: (i) Brutal or inhumane treatment of human subjects is never morally justified. (ii) Risks should be reduced to those necessary to achieve the research objective. It should be determined whether it is in fact necessary to use human subjects at all. Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures. (iii) When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject—or, in some rare cases, to the manifest voluntariness

of the participation). (iv) When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. A number of variables go into such judgments, including the nature and degree of risk, the condition of the particular population involved, and the nature and level of the anticipated benefits. (v) Relevant risks and benefits must be thoroughly arrayed in documents and procedures used in the Informed Consent process.

3. Selection of Subjects.— Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects. Justice is relevant to the selection of subjects of research at two levels: the social and the individual. Individual justice in the selection of subjects would require that researchers exhibit fairness: thus, they should not offer potentially beneficial research on to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that a distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons. Thus, it can be considered a matter of social justice that there is an order of preference in the selection of classes of subjects (e.g., adults before children) and that some classes of potential subjects (e.g., the institutionalized mentally infirm or prisoners) may be involved as research subjects, if at all, only on certain conditions.

Injustice may appear in the selection of subjects, even if individual subjects are selected fairly by investigators and treated fairly in the course of research. This injustice arises from social, racial, sexual and cultural biases institutionalized in society. Thus, even if individual researchers are treating their research subjects fairly, and even if IRBs are taking care to assure that subjects are selected fairly within a particular institution, unjust social patterns may nevertheless appear in the overall distribution of the burdens and benefits of research. Although individual institutions or investigators may not be able to resolve a problem that is pervasive in their social setting, they can consider distributive justice in selecting research subjects. Some populations, especially institutionalized ones, are already burdened in many ways by their infirmities and environments.

When research is proposed that involves risks and does not include a therapeutic

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component, other less burdened classes of persons should be called upon first to accept these risks of research, except where the research is directly related to the specific conditions of the class involved. Also, even though public funds for research may often flow in the same directions as public funds for health care, it seems unfair that populations dependent on public health care constitute a pool of preferred research subjects if more advantaged populations are likely to be the recipients of the benefits. One special instance of injustice results from the involvement of vulnerable subjects. Certain groups, such as racial minorities, the economically disadvantaged, the very sick, and the institutionalized may continually be sought as research subjects, owing to their

ready availability in settings where research is conducted. Given their dependent status and their frequently compromised capacity for free consent, they should be protected against the danger of being involved in research solely for administrative convenience, or because they are easy to manipulate as a result of their illness or socioeconomic condition.

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8:45 am] BILLING CODE 4110-
08-M



**H+H HUMAN SUBJECT RESEARCH PROTECTIONS PROGRAM
POLICIES AND PROCEDURES**

EXHIBIT 2

FACILITY COMMITMENT FORM

The New York City Health and Hospitals Corporation (“H+H”) seeks to support and promote research, thus fostering an environment where research is supported by all parties. This can be done by individual efforts or by partnering with academic scientists and clinical researchers while adhering to precepts to protect human research participants’ rights and safety, with the ultimate goal of having H+H facilities provide access to cutting edge therapies and to promote and protect the health of New Yorkers. To achieve this goal, it is imperative that each Facility in which research is conducted or that provides resources for research commit to assuring a supportive and compliant environment for the conduct of research.

To that end, the undersigned hereby certify that they have read the H+H Human Subject Research Protections Program Policies and Procedures, Operating Procedure No. 180-9 (the “Policies and Procedures”) and will comply with these Policies and Procedures.

Facility Name

FACILITY EXECUTIVE DIRECTOR

Signature of Executive Director

Date

Printed Name

FACILITY MEDICAL DIRECTOR

Signature of Medical Director

Date

Printed Name

EXHIBIT 3

REGULATIONS PERTAINING TO HUMAN SUBJECTS PROTECTION

21 C.F.R. Part 56, Institutional Review Boards.

21 C.F.R. Part 50, Protection of Human Subjects.

21 C.F.R. Part 312, Investigational New Drug Application.

21 C.F.R. Part 812, Investigational Device Exemptions.

34 C.F.R. Parts 356, Disability and Rehabilitation Research.

34 C.F.R. Part 98, Protection of Pupil Rights Amendment (PPRA); Student Rights in Research, Experimental Programs, and Testing.

34 C.F.R. Part 99, Family Educational Rights and Privacy Act (FERPA).

45 C.F.R. Part 46, Protection of Human Subjects.

45 C.F.R. Parts 160 and 164, Standards for Privacy of Individually Identifiable Health Information; Security Standards for the Protection of Electronic Protected Health Information (HIPAA Privacy and Security Rules).

42 U.S.C. § 290dd-2 and its implementing regulations at 42 C.F.R. Part 2, confidentiality of federally assisted drug and alcohol program records.

The implementing regulations of the 21 U.S.C. § 823(g)(1)(a) found at 42 C.F.R. § 8.11[f][3], confidentiality of records maintained by a certified opioid treatment program.

42 U.S.C. § 17921 et seq., HITECH provisions of the American Recovery and Reinvestment Act of 2009.

42 C.F.R. Part 93, research misconduct policies governing Public Health Service grants.

Article 24-A of the New York State Public Health Law.

Public Health Law Article 32-A and its implementing regulations at 10 NYCRR subpart 61-1, Recombinant DNA Experiments.

Mental Hygiene Law §§ 22.05[b] and 33.13[c], [e], confidentiality of clinical records.

Civil Rights Law § 79-1, confidentiality of predisposition genetic testing information.

Public Health Law § 18[6], confidentiality of patient information.

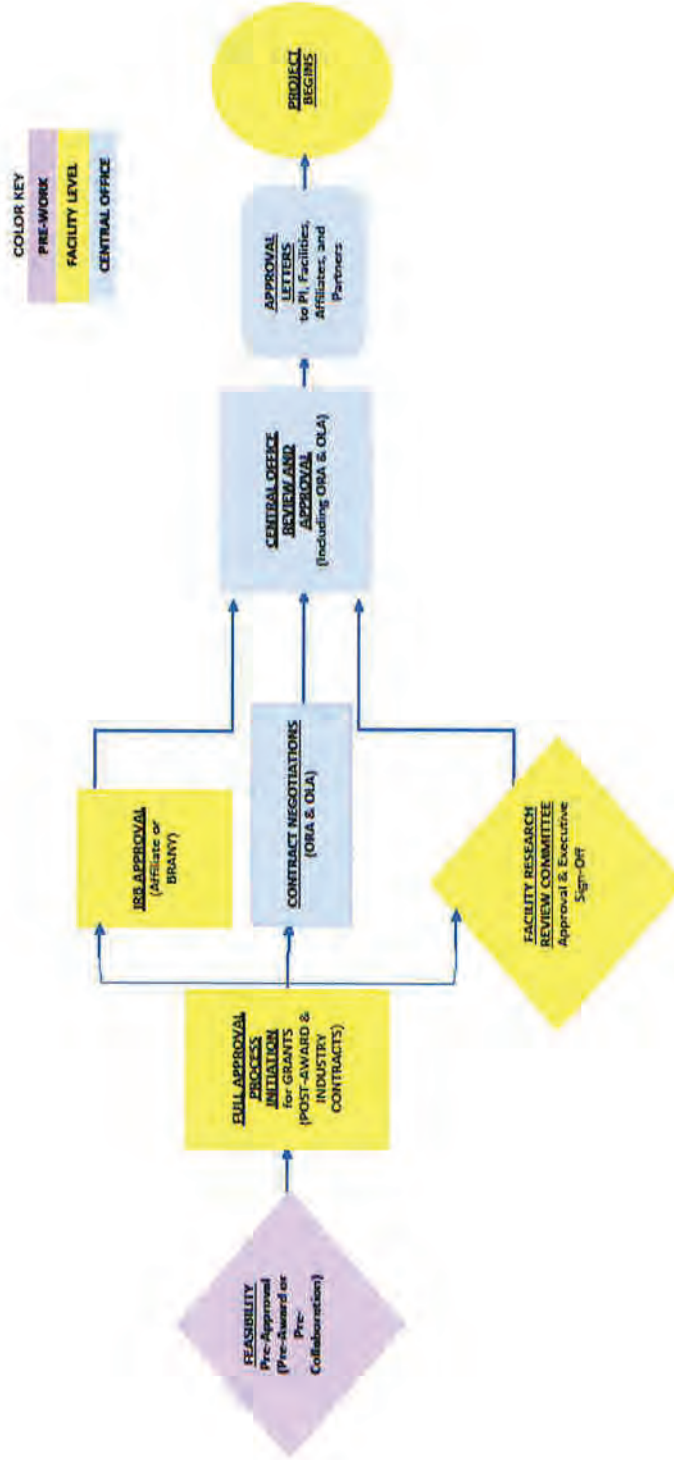
Public Health Law Article 27-F, HIV/AIDS related information.

10 NYCRR § 405.7, patient rights with respect to human subject research.

New York Public Health Law Article 29-Cc (The Family Health Care Decisions Act).

EXHIBIT 4

RESEARCH PROCESS MAP



3933042-1 012030.0105

EXHIBIT 5

RESEARCH AGREEMENT REQUIRED CONTRACT PROVISIONS

The following provisions are required to be included in Research agreements. This is to provide Principal Investigators with a general understanding of what is acceptable to H+H to be in an agreement with a Sponsor. Principal Investigators should not rely on this information as a substitute for obtaining review by the Office of Research Administration and approval by the Office of Legal Affairs.

1. Confidentiality.

(a) H+H does not permit the following to be deemed confidential as part of any agreement with a Sponsor:

(i) The general nature of the inquiry to be conducted as part of the Research Project,

(ii) The identity of the Sponsor, or

(iii) Research results, to the extent necessary to be disclosed for patient or public safety concerns.

(b) All contractual agreements with Sponsors must retain the right of H+H to disclose Research Project Data at any time as necessary for patient or public safety concerns.

2. Publication. H+H requires that all Research Project Data be freely publishable after a short period for review and comment by the Sponsor. In no event shall the Sponsor have the right to edit or alter the manuscript unless to delete confidential language. The total period of delay for Sponsor's review and comment and patent filing purposes cannot exceed ninety (90) days. Also, there is some allowance for additional delays for multi-center Research Projects. Please see Section 10 of this Policies and Procedure for more information.

3. Subject Injury. H+H's template subject injury language is as follows:

"Sponsor agrees that it, and not H+H, is responsible for the costs of diagnosis, care and treatment of any undesirable side effects, adverse reactions, illness or injury to a participant in the Study, which in the reasonable judgment of the Principal Investigator or H+H result from participation in the Study, except for such costs that arise directly from (i) the negligent activities, reckless misconduct or intentional misconduct of H+H, the Principal Investigator or his/her staff or (ii) their failure to adhere to the terms of the Protocol. This section is not intended to create any third-party contractual benefit for any participants in the Study."

4. Intellectual Property. H+H requires that ownership of all Inventions resides with H+H except for inventions resulting from Sponsor-authored Research Protocols.

5. Use of Name and Publicity. Use of H+H's name, logo, etc., for publicity or promotional purposes requires prior written consent.

EXHIBIT 6
OFFICE OF CHILDREN AND FAMILY SERVICES (OCFS) RESEARCH APPROVAL
GUIDELINES

(JUNE 2016)



EXHIBIT 7

NYC ADMINISTRATION FOR CHILDREN'S SERVICES (ACS) RESEARCH PROPOSAL SUBMISSION GUIDELINES



ACS Research
Proposal Submission

EXHIBIT 8

GUIDANCE FOR LEGALLY AUTHORIZED REPRESENTATIVES ENROLLING INDIVIDUALS WITH IMPAIRED DECISION-MAKING ABILITY IN RESEARCH STUDIES

You are acting as the legally authorized representative for an individual who lacks the decisional capacity to consent to take part in a research study. You have the ability to consent to or to refuse that person's participation in the research study. This guide is to help you decide whether or not to enroll that person into the research study. We will refer to the person for whom you are the legally authorized representative as the "**potential participant**".

When determining whether the potential participant should participate in the research study, you should consider:

First: What you know about this person and his/her attitude to research in general and research in this particular medical area in specific. You should also take into account the specifics of the research study and how this person might respond to any interventions in the study such as needle sticks or other such study interventions.

Second: Written Instructions. Look to any written instructions as important reflections of deeply held values. Prior written instructions, however, are unlikely to address the specifics of this research study.

Third: Express Prior Wishes. You should consider any other prior wishes and preferences about research that were expressed by the potential participant, noting, again, that the details of this research study were probably not considered.

Forth: If no prior wishes were expressed, or if the wishes were not related to the facts of this research study, you should consider the following principles to help decide whether enrollment in a research study is in the best interest of the potential participant:

Direct Benefit Exists: If there is a possible benefit to the potential participant by being part of the research study, you should understand this possible benefit and weigh it against any risks to the participant. In making the risk/benefit assessment you should consider the following: (1) the individual's diagnosis; (2) the possible short-and long-term effects on the physical or mental well-being of the participant; (3) the expected degree of physical pain or discomfort, psychological distress, and any loss of dignity that may result from participation; (4) whether there are treatment alternatives to research participation available; and (5) the risks, benefits, and potential side effects of participation in research as compared to those of standard treatment. You should ask the doctor about the standard treatment to determine if there is any benefit that might be added to the potential participant by participating in the research study or whether there might be no benefit to such participation.

No Direct Benefit Exists: Sometimes no direct benefit to the potential participant exists but enrolling in the research study could advance research to find a cure, new treatments or new therapies. Even though there is no direct benefit to the potential participant you may still enroll the potential participant into a research study *if you believe that is what he or she would have done*. To make that decision you can look at factors such as indicators of his or her beliefs about medical research, including prior research participation, general statements or attitudes about research participation, or specific moral or religious convictions that may have some bearing on medical research together with an understanding of the expected degree of physical pain or discomfort, psychological distress, and any loss of dignity that may result from participation.

Based on these factors you may determine whether the potential participant might have chosen to enroll in the research study if he or she could make the decision.

Fourth: Your Continuing Role: Finally, you should understand that you have a continuing role and responsibilities regarding the participant and the research study. It is expected that you would be available on an ongoing basis once the potential participant is enrolled in the research study. You should be accessible to both the participant and researchers to oversee participation, communicate with researchers and the participant, and make additional decisions where necessary. It is imperative that you serve as an ongoing active advocate to the participant by ensuring that you remain consistently involved in the study.

I, the legally authorized representative for _____, have received a copy of the “*Guidance for Legally Authorized Representatives Enrolling Decisionally Incapacitated Individuals in Research Studies*” and have had an opportunity to review it and ask questions.

Legally Authorized Representative’s Name

Legally Authorized Representative’s Signature

Date

EXHIBIT 9

CONFLICT OF INTEREST FORM DISCLOSURE OF SIGNIFICANT FINANCIAL INTERESTS AND OBLIGATIONS

PART I

All H+H investigators seeking external sponsored funding to conduct scholarly activities are required to complete and file a signed Disclosure of Significant Financial Interests and Obligations each year. Each investigator must complete this form before a proposal can be endorsed for submission.

Subpart A

Specific Instructions: Place a check in the appropriate column for each question.

Investigator Name: _____

Research Project Title: _____

Facility/Department: _____

Questions	Yes	No
1) Interests in Publically Traded Entities. Have you, your spouse or dependent child(ren) received in the last 12 months any remuneration (salary, consulting fees, honoraria, paid authorships, or other payment not related to salary) from, or hold an equity interest (stock, stock options, or other ownership interest) in any publically traded entity that, when aggregated, exceeds \$5,000?	<input type="checkbox"/>	<input type="checkbox"/>
2) Interests in Non-Publically Traded Entities. 2a) Have you, your spouse or dependent child(ren) received in the last 12 months any remuneration (salary, consulting fees, honoraria, paid authorships, or other payment not related to salary) from any non-publically traded entity that, when aggregated, exceeds \$5,000? 2b) Do you, your spouse or dependent child(ren) hold an equity interest (stock, stock options, or other ownership interest) in any non-publically traded entity?	<input type="checkbox"/> <input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/>
3) Intellectual Property. Do you, your spouse or dependent child(ren) have intellectual property rights or interests (patents, copyrights) that generate income (such as royalties)?	<input type="checkbox"/>	<input type="checkbox"/>
4) Travel. Have you engaged in any reimbursed or sponsored travel (that which is directly paid by the sponsor on your behalf) related to a research project funded by external sponsored funding?	<input type="checkbox"/>	<input type="checkbox"/>

If you answered ***No*** to **ALL** of questions 1 through 4 above, your Disclosure is complete; you do not have to fill out Subpart B or submit Part II. Please sign and date the certification below and forward to the Office of Research Administration.

If you answered ***Yes*** to **ANY** of questions 1 through 4 above, please continue on to Subpart B below.

Subpart B

Specific Instructions: Place a check in the appropriate column for each question. Once every question is answered, the investigator must certify the information by signing the bottom of the form.

5) Are any of the interests described in questions 1 through 4 above held by you, your spouse or dependent child(ren) related to your activities or responsibilities in connection with your sponsored research?	<input type="checkbox"/>	<input type="checkbox"/>
6) Is it reasonable to anticipate that your financial interest could be directly and significantly affected by the design, conduct, or reporting of your sponsored program activity?	<input type="checkbox"/>	<input type="checkbox"/>

If you answered “**No**” to **BOTH** questions 5 and 6 above, your Disclosure is complete; you do not have to submit Part II. Please sign and date the certification below and forward to the Office of Research Administration.

If you answered “**Yes**” to **EITHER** question 5 or 6 above, please complete a separate Part II for **every** outside organization with which you have the relationship(s) indicated in Subpart A above.

Investigator Certification:

- I have read and understood the H+H Operating Procedure No.: 180-9: Human Subject Research Protection Program Policies & Procedures section on Conflicts of Interest.
- I agree to file a new or updated Disclosure of Significant Financial Interests and Obligations form if the answer to any of the above questions changes.
- I certify that the answers to the declaration are accurate and truthful to the best of my knowledge.

Signature: _____

Date: _____

PART II

Complete Part II only if you answered, "YES" to at least one of the questions in Subpart B of Part I.

Attach one Part II form for each organization with which you have the relationship(s) indicated in Part I.

Investigator Name: _____

Number of Part II forms submitted: ___, of which, this is number ___:

1. Name of organization: _____

2. Financial relationship(s) with the organization, other than an independent scientific advisory board (check all that apply):

<input type="checkbox"/> Consultant	<input type="checkbox"/>		<input type="checkbox"/> Employee
<input type="checkbox"/> Equity Interest	<input type="checkbox"/>	Recipient of	<input type="checkbox"/> Honoraria
<input type="checkbox"/> Recipient of Royalties	<input type="checkbox"/>	Travel	
<input type="checkbox"/> Other (Describe): _____			

3. The financial relationship is between the organization and (check all that apply):

<input type="checkbox"/>	Self
<input type="checkbox"/>	Spouse
<input type="checkbox"/>	Dependent Child(ren)

4. Have you received in the last twelve (12) months, or do you expect to receive in the next twelve (12) months, payments for salary, director's fees, consulting, honoraria, royalties, or any other payments that when aggregated with payments from this organization to your spouse and/or dependent child(ren) will exceed \$5,000?

Y ☐ N ☐

5. Have you had in the last twelve (12) months or do you anticipate having in the next twelve (12) months, stock, stock options, or other equity interests in the organization which, when aggregated with those of your spouse and dependent child(ren) in this organization, have a fair market value exceeding \$5000?

Y ☐ N ☐

6. What relationship, if any, is there between the business or activities of the organization and your current or planned areas of research?

7. Are you a member of any independent scientific advisory board from which the value of the Remuneration when aggregated in the twelve months preceding the disclosure exceeds \$5,000?

Y ☐ N ☐

If yes, please explain: _____

EXHIBIT 10

INVENTION DISCLOSURE FORM

Completed form should be submitted via:

USPS:

Facsimile:

E-mail:

Title of Invention*

* "Invention" means any discovery or invention (whether or not patentable) created, conceived or reduced to practice as a result of Research including, but not limited to, all copyright and copyrightable material (unless published in academic or scholarly media or otherwise in the public domain), and all such intellectual property rights inhering in tangible research property. "Research" means an activity that meets any of the definitions of research stated in DHHS regulations, FDA regulations, or New York Public Health Law, each as may be amended from time to time, and which uses H+H patients, facilities, staff or resources or which is conducted at an H+H Facility.

Brief Description of Invention**

--

****For a complete description please include an Attachment with the following:**

Background of the Invention and any related technologies (the problem the invention solves)
Are there existing products that address the same problem that the Invention solves? Please name and describe them.

List all relevant publications, patents and competing inventors or labs that you are aware of.

Unique features of the invention

List all of the features that distinguish the invention over the related technologies.

Detailed description of the invention including:

How to make and use the invention

Best mode of making the invention

Drawings or pictures of all aspects of the invention

Possible alternative versions of the invention

Probable uses of the invention

Funding and/or Sponsorship: Please include all outside agencies, foundations, organizations, or companies and the applicable contract or grant number(s) that provided funding to any inventor for the research that led to the invention. Please also include any companies that have supplied materials in exchange for intellectual property rights. **(If there is no funding or sponsorship, then mark *None*.)**

None	US Government	Commercial/Private	H+H	Personal	Other
Name of Sponsor		Sponsor Project ID			

Was any **third party Software** included in the invention? **Y N** If yes, please provide the information on the source of the third party Software and any constraints on its use in the current invention.

Record of Invention (If no information is available, then mark *None*.)

1.	Date of Conception:	Documented? Y N	Form of documentation:
			Location of documentation:
2.	Invention Reduced to Practice? Y N	Date of First Reduction to Practice:	Prototype Available? Y N
None			

Publication(s): Please provide a copy of all materials disclosed or anticipated to be disclosed in the near future in any of the following forms. (If no information is available or no plan for disclosure in the near future, please state "*None*".)

Article Submittal:	Date:	Journal:	Publication Date:	Estimated or actual?
Oral Disclosure:	Date:	Occasion:	Handouts? Y N	
Thesis:	Date:	Shelved: Y Date: N	Web publication: Y N	
News Release:	Date:	Publication:		
Web Site:	Date:	URL:		
Discussion with Industry Representatives:	Date:	Venue:		
Poster presentation:	Date:	Occasion:	Published Abstract: Y N	
			Citation:	
None				

Commercial Interest: Please list the specific contacts if you have them, or simply list some companies that are the type of company that you think might be interested in this invention. (If no information is available, then mark *None*.)

Company	City/State	Contact Person	Title of Contact Person
None			

Inventor Information Section: Please list all inventors. Inventorship is a matter of law and is different from authorship on a scientific paper. Per US Patent Law, an inventor is someone who contributed **intellectually to the conception of the invention as claimed in a patent application**. Genuine inventorship therefore also depends on the specific claims to be made in a patent application on the invention. Neither the expression of the need of an invention, the funding of a project, supervising the execution of a project, nor performing work as a “pair of hands” at other’s instructions to reduce an invention to practice is sufficient to qualify someone as an inventor.

If you have one or more collaborators, whether at H+H or at other institutions, and you are not absolutely sure they are qualified as inventors according to US patent law, it is advisable to not simply assume all of them as inventors but to list them in a separate attachment to this disclosure (each with contact information) and to describe each individual’s contribution to the work from which this invention arose so that H+H and the Office of Legal Affairs may have the opportunity to, based on the facts presented, determine each individual’s contributions to the claims in the eventual patent application for the invention H+H may file.

VIIA. H+H Inventors:

Name of Primary Contact for H+H regarding this invention: _____

H+H Inventor Data (1)

Name:		Title:	
H+H Address:		Division:	
		H+H phone:	
e-mail:		H+H fax:	
Home Address:		Country of citizenship:	
Home phone:			

H+H Inventor Data (2)

Name:		Title:	
H+H Address:		Division:	
		H+H phone:	

e-mail:		H+H fax:	
Home Address:		Country of citizenship:	
Home phone:			

H+H Inventor Data (3)

Name:		Title:	
H+H Address:		Division:	
		H+H phone:	
e-mail:		H+H fax:	
Home Address:		Country of citizenship:	
Home phone:			

***Note: If there are more than three H+H inventors, please provide additional information on a supplemental sheet.**

VIIIB. Non-H+H Inventors

Institution/Company/Organization	Non-H+H Inventor Name	Address/Email
None		

VIIIC. H+H Inventor Signature(s): Per the H+H Research Policy, I (we) hereby disclose this invention to New York City Health and Hospitals Corporation ("H+H") and declare that this invention disclosure is complete and accurate to the best of my (our) knowledge.

Inventor Signature	Date	Witness Signature	Date
(1)			
(2)			
(3)			

Please check one of the following boxes:

I (We) agree this invention is an H+H invention and hereby assign all rights, title and interests in and to this invention to H+H. I (we) further agree to execute all documents as requested to assign my (our) rights to H+H in and to any patent application or other statutory form of intellectual property protection filed in connection with this disclosure, and to cooperate with H+H's Office of Legal Affairs in securing protection of the disclosed invention.

I (We) do not believe this is a H+H invention as defined in H+H Research Policy and therefore should not be assigned to H+H. I (We) hereby request the Office of Legal Affairs to make a determination of the proper ownership of this invention based on the information I (we) provided in the attachment to this Disclosure Form.

[Note: If you believe the invention should NOT be assigned to H+H Office of Legal Affairs for whatever reason(s), you should check the box immediately above this paragraph and attach to this Invention Disclosure form at the time of its submission to H+H Office of Legal Affairs a written statement of all the reasons/justifications to support your request. H+H Office of Legal Affairs will then examine your request and make a determination based on the information you present as well as other information it may obtain from the various official records.

EXHIBIT 11

OHRP QA SELF-ASSESSMENT TOOL



OHRP QA
SELF-ASSESSMENT T

INVESTIGATIONAL DRUG ACCOUNTABILITY LOG

[illegible]

EXHIBIT 13

INVESTIGATIONAL DRUGS AND SUPPLIES LETTER OF UNDERSTANDING (LOU)

Medical Facility Name: _____

Protocol or Study Name: _____

This letter reflects the understanding between _____ (hereinafter referred to as "Health and Hospitals Corporation (H+H) Affiliate") and the H+H Medical Facility at _____ regarding the circumstances under which the H+H Affiliate agrees to provide study drug/device to the H+H Medical Facility for the protocol or study referenced above (hereinafter referred to as "Protocol" or "Study"). A copy of the Protocol, dated ____ / ____ / ____, is attached and incorporated herein by reference.

The H+H Medical facility Pharmacy Service at _____ serves as a liaison between the H+H Affiliate and the H+H investigator and acts as the central control and distribution center for donated drugs/devices for the Study. Facility Pharmacist must provide guidance and information regarding study drugs as well as serving as a conduit for communications between the H+H Affiliate and the Food and Drug Administration, when appropriate. The H+H Affiliate provides **[Insert drug name and strength]** and matching placebo (hereinafter referred to as "Study Drug") for the Study in accordance with the following provisions.

The H+H Medical facility at _____ and the H+H Affiliate have agreed upon the following operating procedures in connection with the Study and this Letter of Understanding:

1. **Conduct of the Study.** The H+H Medical Facility at _____ will conduct the Study in accordance with the terms of Protocol and within H+H guidelines with the participation of the H+H Affiliate.
2. **Drug Supply, Distribution, and Accountability.** The H+H Affiliate will supply Study Drug for the duration of the Study, free of charge, and will include in planning allowances for wastage that may unavoidably occur during dispensing. The H+H Affiliate will provide shipment of Study Drug directly to the Pharmacy Service in accordance with the schedule agreed to by both parties. The Pharmacy Service will label and dispense Study Drug and keep all records of drug disposition. The Pharmacy Service warrants that in its processes the Study Drug shall not be adulterated or misbranded, in accordance with the Food, Drug and Cosmetic Act. Pharmacy Service agrees to use the Study Drug supplied by H+H Affiliate only for the investigational purposes authorized under the Protocol. No other use of the drug will be permitted by Pharmacy Service. In the event that the Pharmacy Service has unused Study Drug at the time the Study is completed or terminated, the Pharmacy Service will dispose of Study Drug in accordance with operating procedures outlined by the H+H Affiliate.
3. **Safety Information Reporting.** The Principal Investigator is responsible for reporting adverse events with respect to Study Drug to the H+H Affiliate and/or Food and Drug Administration in conformance with all applicable laws, rules, and regulations in effect.

(a) The Principal Investigator must provide to the H+H Affiliate any information on any serious adverse event, side effect, injury, toxicity, sensitivity reaction or any unexpected incidence and the severity thereof related to the Study Drug that is associated with its “clinical” use in accordance with the Protocol. “Serious Adverse Events,” as used in this context, have the meaning ascribed thereto in the Protocol.

(b) It is understood and agreed that these adverse events reporting requirement provisions are based upon the H+H Affiliate’s respective policies and procedures and regulatory reporting requirements. Accordingly, in the event of changes to H+H Affiliate’s policies and procedures for adverse events reporting, the principal investigator agrees to comply with such revised notification requirements as reasonably requested in writing by the H+H Affiliate. This is provided that the scope and extent of activity and undertakings are not materially increased. The H+H Affiliate agrees to pay all costs associated with this request.

4. Early Study Termination. The Study may be terminated at any time by the Institutional Review Board for safety or efficacy reasons if it is thought to be in the best interests of the patients. Either H+H or the H+H Affiliate may withdraw support from the Study with 90 days written notice only if this agreement has been violated.

5. Patient Confidentiality. Patient confidentiality must be maintained at all times in accordance with applicable law and H+H policy. Reports issued for public distribution or to the H+H Affiliate will contain only aggregate data with all patient identifiers removed.

6. Selection of Participants. The H+H Medical Facility at _____ is responsible for all decisions concerning the selection and/or discontinuation of participants in the Study.

7. Record Retention. The H+H Medical Facility at _____ must retain all records related to the Study (according to H+H policy and procedure) for a minimum period of 3 years from the date of the last patient follow-up. At that point the Study records will be evaluated for archiving.

8. Term of Agreement. This agreement shall be effective as of the date last signed below and shall expire upon completion of all activities related to the Study as defined by the submission of the final Study report to the H+H Affiliate and the primary publication of the Study results.

9. Modification to Agreement. This agreement may be amended or superseded only by a written agreement of the parties.

10. Approval. The following signatures indicate approval of the terms of this letter of understanding.

(Remainder of page intentionally left blank.)

(Name and Signature of the Principal Investigator) (Date)

(Name of the H+H Affiliate)

(Name and Signature of the H+H Facility CMO) (Date)

(Name of the H+H Facility)

EXHIBIT 14

MATERIALS TRANSFER AGREEMENT TEMPLATE

THIS MATERIAL TRANSFER AGREEMENT is entered into on [INSERT DATE] (“Effective Date”) by and between the New York City Health and Hospitals Corporation (“H+H”) and Dr. _____, MD at [NAME OF OTHER INSTITUTION] (hereinafter collectively referred to as “Recipient”) in connection with the transfer of biological materials (the “Materials”) identified in the Research Project, attached hereto as Exhibit A.

Whereas, Recipient desires to obtain Materials from H+H and H+H is willing to allow the transfer of such Materials to Recipient for the purposes stated in this Agreement.

The parties hereby agree to the following terms and conditions:

1. The Materials shall be used exclusively for non-commercial research by Recipient for the Research Project. Materials will not be used for in vivo testing in human subjects. Recipient assumes all risk and responsibility in connection with the receipt, handling, storage, disposal, transfer and use of the Materials including, without limitation, taking all appropriate safety and handling precautions to minimize health or environmental risk. Recipient agrees that any activity undertaken with the Materials and any derivatives will be in compliance with all applicable Federal, State and local laws and regulations, including, but not limited to, the Health Insurance Portability and Accountability Act of 1996 (HIPAA), the Genetic Information Nondiscrimination Act (GINA) and the Health Information Technology Economic Clinical .
2. THE MATERIAL IS NOT FOR USE IN HUMAN SUBJECTS.
3. The Materials and any modifications and derivatives are the property of H+H.
4. Recipient shall not sell or otherwise distribute Materials to a third party for any purpose. This Agreement and the resulting transfer of Material constitute a non-exclusive license to use the Material solely for the research purposes described in Exhibit A. Except as explicitly permitted by the Informed Consent form taken from each subject as part of the Research Project, Recipient shall not use Materials for any products or processes for profit-making or commercial purposes.
5. The parties acknowledge that Data from Recipient’s use of the Materials shall be furnished to the H+H for use by H+H and its employees, subcontractors and agents. “Data” shall refer to all patient data, genomic data, analytic data, research data and other data collected, developed or derived by the Recipient from the activities carried out under this Agreement pursuant to the applicable Research Project (including, without limitation, all research, pre-clinical and clinical data).
6. This Agreement is not assignable.
7. H+H have made, or may make Materials available to others, both profit and non-profit.

8. Recipient agrees to provide H+H with a copy of any publications which contain experimental results obtained from the use of the Materials. Recipient will acknowledge H+H as the source of the Materials in all publications and patent applications containing any data or information about the Material unless H+H indicates otherwise. H+H retains all right, title and interest in the trademarks registered or owned by H+H and any and all H+H catalog numbers or H+H specific designations of Materials.

9. Recipient shall notify H+H, in confidence, of any inventions that are conceived and reduced to practice through the use of the Materials ("Invention"). Recipient and H+H shall enter into good faith negotiations to negotiate a license with respect to any Invention Recipient will arrange the return to H+H or disposal of all unused Material whenever investigation for which it has been supplied discontinues or is terminated

10. The Materials and any data or technical assistance hereunder provided are AS IS AND WITHOUT ANY WARRANTIES, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION, WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR USE. H+H MAKES NO REPRESENTATION AND PROVIDES NO WARRANT THAT THE USE OF THE MATERIAL WILL NOT INFRINGE ANY PATENT OR OTHER PROPRIETARY RIGHT.

(a) Recipient is responsible for all taxes, duties, tariffs and permit fees assessed in connection with these Materials. Recipient shall, upon demand, pay to H+H an amount equal to any such tax(es), duties, tariffs and permit fees actually paid or required to be collected or paid by H+H and/or its designee.

(b) H+H will package the Material for shipping in accordance with applicable laws and regulations. All Materials are shipped Free on Board (FOB) point of shipment, freight prepaid via carrier of our choice and added to your invoice. If the Material is lost or damaged during shipment, H+H will replace such Material at no additional charge, provided that you have reported lost or damaged shipments to the applicable carrier and notified H+H in writing within fourteen (14) days from the shipment date. Each invoice will be mailed the following day after Materials are shipped from the point of shipment.

11. Recipient agrees to indemnify, defend and hold harmless H+H and its trustees, officers, directors, staff, agents and representatives against all damages, expenses (including without limitation legal expenses), claims, demands, suits or other actions arising from Recipient's acceptance, use, receipt, handling, storage, transfer, disposal and other activities relating to the Materials and their derivatives except insofar as such claims or liability arise out of the gross negligence or wrongdoing of H+H and its trustees, officers, directors, staff, agents and representatives.

Accepted by:

[OTHER INSTITUTION]

Authorized Officer: _____

Title: _____

Signature: _____

Date: _____

New York City Health and Hospitals Corporation

Authorized Officer: _____

Title: _____

Signature: _____

Date: _____

EXHIBIT 15

INFORMED CONSENT FOR RESEARCH INVOLVING GENETIC TESTING

(The information below can be incorporated into a general consent, or can be used as a separate consent along with a general consent. If necessary, translate into language of subject.)

Research Project Title:	Patient Name:
Research Project #:	Patient Address:
Principal Investigator:	

The New York City Health and Hospitals Corporation (H+H) requires your written, Informed Consent to perform genetic testing for this specific research project and any possible future research either related to this study or not. If you decide not to participate in this study, your regular care will not be affected nor will your relations with H+H, your physicians, or other personnel. In addition, you will not lose any of the benefits to which you are entitled.

By signing this consent form, you agree to give your samples to H+H for research purposes as described below. You may wish to speak with a professional genetic counselor before signing this consent form to understand the testing and what the results mean.

	Initials
<ul style="list-style-type: none"> • <u>General Description of the Genetic Test:</u> <p>The genetic test(s) will be done using the following sample: _____.</p> <p>The test(s) being ordered is/are _____.</p>	<div style="border: 1px solid black; width: 60px; height: 20px; margin: 0 auto;"></div>
<ul style="list-style-type: none"> • <u>Purpose of the Test:</u> <p>This testing is being conducted as part of the Research Project to determine: _____.</p> <p><i>[Include a statement of the purpose of the test.]</i></p>	<div style="border: 1px solid black; width: 60px; height: 20px; margin: 0 auto;"></div>
<ul style="list-style-type: none"> • <u>Statement regarding test result:</u> A positive test may indicate that you are predisposed to or that you have the condition being tested for. If this is the case, you may wish to have further independent testing, consult your physician, or speak with a genetic counselor. 	<div style="border: 1px solid black; width: 60px; height: 20px; margin: 0 auto;"></div>

<ul style="list-style-type: none"> • <u>Level of Certainty:</u> A positive test result is ____% accurate in predicting whether you have or are predisposed to the condition being tested for. <i>[If the level of certainty is unknown delete this sentence.]</i> 	<input type="text"/>
<ul style="list-style-type: none"> • <u>General Description of each specific disease or condition tested for:</u> <i>[list each specific disease or condition tested for]</i> 	<input type="text"/>
<ul style="list-style-type: none"> • <u>Other tests:</u> No tests other than those authorized by you shall be performed on the sample. 	<input type="text"/>
<ul style="list-style-type: none"> • <u>Persons, or categories of persons, or organizations to which the test results may be released:</u> To the extent permitted by law, under no circumstances will any information linking you to specific test results be disclosed to any individual or organization without your written consent. The results from the genetic tests may be disclosed to the following individuals or groups: <i>[Include a list of persons/entities/groups that may receive the results from the genetic tests]</i> 	<input type="text"/>
<ul style="list-style-type: none"> • <u>Disclosure by H+H for certain purposes:</u> You consent to H+H disclosing your results for your treatment purposes, to receive payment for services rendered to you and for H+H's operations relating to health care. 	<input type="text"/>
I consent to genetic testing on my samples as part of the Research Project.	
<u>Storage of samples:</u> the sample will be destroyed at the end of the Research Project unless you agree to a longer retention period. Please select one of the following:	<input type="text"/>
<u>Use of Samples:</u> The samples that you give to H+H could one day lead to discoveries using methods and tests not yet developed. To that end, H+H would like to keep the samples for as long as they are deemed useful for research purposes. This research could potentially be used for purposes not specified above. However, samples that you give will be destroyed at the end of the testing process unless you consent to longer period of retention.	<input type="text"/>
<u>Consent to Use and Store Sample:</u>	

Yes, I consent to the storage of the samples by H+H to keep the samples for as long as they are deemed useful for research purposes and use of my sample in both unspecified research to be done in the future as well as the Research Project described above.

Yes, I consent to the storage of the samples by H+H for _____ years after which they will be destroyed and I consent to the use of my sample in both unspecified research to be done in the future as well as the Research Project described above.

No, I do not consent to the storage of the samples and request that they be destroyed immediately upon completion of the Research Project.

You can Withdraw Consent: You have the right to withdraw your consent to use your samples at any time, and may request that the samples you give to H+H [or sponsor, if applicable] be destroyed. If you choose to do so, contact your study doctor, [*name of Principal Investigator*], at xxx-xxx-xxxx. Although you are free to withdraw your consent, it is possible the samples may have already been used for research purposes and data derived from such research will not be destroyed. In that event, H+H [or sponsor, if applicable] will promptly destroy any remaining samples.

☐

Policies And Procedures To Protect Your Confidentiality

Your information will be kept confidential in accordance with State and Federal law.

[*Describe the specific confidentiality procedures of the study.*]

[*Based on the structure of the study, include one of the following two statements:*]

(1) The samples will be permanently stripped of information that could identify you. (OR)

(2) H+H uses a coding system that protects the identity of individuals who provide samples. The coding system has been reviewed and approved by the Institutional Review Board.

☐

Sharing Samples With Other Investigators:

Yes, I will allow H+H researchers to share the samples with other investigators for their research which may be unrelated to the Research Project described above.

No, I will not allow H+H researchers to share the samples with other investigators.

<p>A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:</p> <ul style="list-style-type: none"> • Health insurance companies and group health plans may not request your genetic information that we get from this research. • Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. • Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment. <p>Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Nor does this Federal law prohibit discrimination on the basis of an already manifest genetic disease or disorder.</p>	<input data-bbox="1227 243 1347 296" type="checkbox"/>
<p><i>[Only include the following section “Test Results and Future Contact”, if the research includes genetic testing on identifiable samples]</i></p> <p><u>Test Results and Future Contact:</u> There may be circumstances in the future when H+H would like to contact you regarding the samples that you gave. For example, it is possible that genetic tests will show a link between your genetic information and a disease or condition. Knowing this information may help you make choices about you or your family’s health care. However, some individuals prefer not to know about their genetic information.</p>	<input data-bbox="1216 1119 1336 1171" type="checkbox"/>
<p><u>Risks and Benefits of Future Contact:</u> H+H wants you to know that there may be both risks and benefits to consenting to future contact.</p> <p><u>The potential risks include:</u> You may be upset to learn that you have a greater chance of having a disease or condition. Even if genetic tests show that you do not have a greater risk of disease, you may still be upset if you know that others in your family have that higher risk of disease.</p> <p><u>The potential benefits include:</u> You may benefit from the knowledge that you or your family have a predisposition to a certain disease or condition. This knowledge may help you make informed decisions concerning your lifestyle and health care.</p>	<input data-bbox="1216 1459 1336 1512" type="checkbox"/>

<p>I consent to be contacted in the future for any or all purposes including research purposes, provision of general information about research findings, and information about the tests done on the sample that may benefit my family or me.</p> <p>If you agree to be contacted, please provide your contact information below:</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>I do <u>not</u> consent to be contacted in the future regarding future research on my samples, general information about research findings, or information about the tests done on the sample that may benefit my family or me.</p>	

I have read and fully understood this form, and I consent to genetic testing as part of the Research Project and as described above.

Signature of Individual (or individual's legal representative)

Date _____

ENDNOTES

¹ Final revisions to the Federal Policy for the Protection of Human Subjects (the Common Rule) were published in the Federal Register on January 19, 2017. 82 Fed. Reg. 12, 7149 (January 19, 2017). The final rule was amended to delay the effective and compliance dates on January 22, 2018 and June 19, 2018, respectively. 83 Fed. Reg. 14, 2885 (January 22, 2018); 83 Fed. Reg. 118, 28497 (June 19, 2018).

² The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, available at <http://www.hhs.gov/ohrp/policy/belmont.html>.

³ N.Y. Pub. Health L. § 2444(2).

⁴ OIG Compliance Guidance, available at <http://oig.hhs.gov/compliance/compliance-guidance/index.asp#top>.

⁵ 45 C.F.R. § 46.501; <http://www.hhs.gov/ohrp/assurances/irb/>.

⁶ 21 C.F.R. § 56.106; <http://www.hhs.gov/ohrp/assurances/irb/>.

⁷ DHHS Frequently Asked Questions, *Who may sign as the Signatory Official on a Federalwide Assurance (FWA)?* available at <http://answers.hhs.gov/ohrp/questions/7151>.

⁸ 45 C.F.R. § 46.116; 45 C.F.R. § 46.117.

⁹ 45 C.F.R. § 46.108(a)(4)(i).

¹⁰ 45 C.F.R. Part 46.

¹¹ See Joint Commission Standard LD.01.03.0.

¹² OHRP generally considers private information or specimens to be individually identifiable as defined at 45 C.F.R. § 46.102(e) when they can be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. Conversely, OHRP considers private information or specimens not to be individually identifiable when they cannot be linked to specific individuals by the investigator(s) either directly or indirectly through coding systems. See OHRP's Guidance on Research Involving Coded Private Information or Biological Specimens, available at <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/research-involving-coded-private-information/index.html>.

¹³ Please see H+H HIPAA Clinical Investigation and Research Policy and Guidelines, OP 240-23 at Section 1.5 for more information regarding the responsibilities of the Principal Investigator.

¹⁴ Please see H+H HIPAA Clinical Investigation and Research Policy and Guidelines, OP 240-23 at Section 1.3 for more information regarding the responsibilities of the Principal Investigator.

¹⁵ 42 C.F.R. § 46.102(l).

¹⁶ 21 C.F.R. § 56.102(c).

¹⁷ See, for example, the special provisions for the profession of psychology with respect to the conduct of Research set forth at 8 NYCRR § 29.12(a)(1).

¹⁸ 45 C.F.R. § 46.102(d).

¹⁹ 45 C.F.R. § 46.102(f).

²⁰ 45 C.F.R. § 46.101(b).

²¹ For further information, see: <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/informed-consent/index.html>. As of March 27, 2018, the HHS guidance references the version of the Common Rule that was in place prior to July, 2019.

²² Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (June 21, 2016) available at <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html>.

²³ 45 C.F.R. § 46.116(e), (f); 21 C.F.R. §§ 50.23 and 50.24; New York Public Health Law, Article 24-A, Section 2442.

²⁴ 21 C.F.R. § 46.116(a).

²⁵ 45 C.F.R. § 46.116.

²⁶ 21 C.F.R. §§ 50.25 and 50.20.

²⁷ Under 45 C.F.R. § 46.102(j) and 20 C.F.R. § 50.3(k), “minimal risk” exists where “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.”

²⁸ 45 C.F.R. § 46.116(d).

²⁹ 45 C.F.R. § 46.117.

³⁰ *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, Section III-C-1, p. 16, available at https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf.

³¹ *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, Section I-B, p. 9. available at https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf. New York law uses the term “recombinant DNA”, which means “[deoxyribonucleic acid] molecules which (a) have been formed by joining together [deoxyribonucleic acid] segments in [an environment outside of any cell or cellular organism] and which have the capacity to enter a cell and to replicate in such cell either autonomously or after they have become an integrated part of such cell’s genome; or (b) are the result of a replication of the [deoxyribonucleic acid] molecules described in paragraph (a) of this subdivision.” N.Y. Pub. Health Law § 3221(2).

³² *NIH Guidelines for Research Involving Recombinant Synthetic Nucleic Acid Molecules*, available at https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf.

³³ CDC, *Biosafety in Microbiology and Biomedical Laboratories*, available at <http://www.cdc.gov/biosafety/publications/bmbl5/BMBL.pdf>.

³⁴ NIH and OBA *Frequently Asked Questions about Externally Administered Institutional Biosafety Committees (IBCs)*, available at <https://www.sc.edu/ehs/Biosafety/IBC/FAQs%20about%20Externally%20Administered%20IBCs.pdf>; *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, Section IV-B-1-c, p. 24, available at https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf; 10 NYCRR 61-1.3(a)(1) and (b) (requiring researchers performing recombinant DNA experiments to establish an institutional biosafety committee compliant with state regulations or provide documentation of NIH approval of the experiment); 10 NYCRR 61-1.30(b).

³⁵ *NIH Guidelines for Research Involving Recombinant Synthetic Nucleic Acid Molecules*, at Section IV-B-1-g and h, p. 25, available at https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf; 10 NYCRR 61-1.30(g).

³⁶ N.Y. Pub. Health Law § 3222; 10 NYCRR 61-1.3(a).

³⁷ *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, at Section IV-B-7-b-(6), p. 30, available at https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf.

³⁸ 10 NYCRR 61-1.33(c).

³⁹ *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, Appendix M-I-B, p. 101, available at https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf; 10 NYCRR 61-1.33(b).

⁴⁰ *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, at Appendix M, p. 99, available at https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf.

⁴¹ *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, at Appendix M-I-A (Requirements for Protocol Submission), p. 100-101, available at https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf.

⁴² *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, at Appendix M-I-C (Reporting Requirements), p. 102., available at https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf.

⁴³ *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, at Section IV-B-7-d and e, p. 30, available at https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf; 10 NYCRR 61-1.33(d) and (e).

⁴⁴ 45 C.F.R. §§ 46.401-46.409; 21 C.F.R. Part 50, Subpart D; Chapter 14, Domestic Relations Law, Article 1 §2.

⁴⁵ 45 C.F.R. § 46.407.

⁴⁶ 45 C.F.R. § 46.405-408.

⁴⁷ OHRP Research with Children – FAQs, available at <http://answers.hhs.gov/ohrp/categories/1570>.

⁴⁸ 45 C.F.R. § 46.409; 21 C.F.R. § 50.3(q); N.Y. Soc.Serv.L. § 358-A.

⁴⁹ N.Y. Soc.Serv.L. § 358-A.

⁵⁰ 45 C.F.R. § 46.409(a).

⁵¹ 45 C.F.R. § 46.409(b).

⁵² 45 C.F.R. § 46.408.

⁵³ New York State Office of Children and Family Services (OCFS) Research Approval Guidelines (June, 2016).

⁵⁴ N.Y. Soc.Serv.L. § 372.4-b; New York State Office of Children and Family Services (OCFS) Research Approval Guidelines (June, 2016).

⁵⁵ New York State Office of Children and Family Services (OCFS) Research Approval Guidelines (June, 2016), , at p. 4-5; N.Y. Pub. Health Law § 2442.

⁵⁶ New York City Administration for Children's Services: Research Proposal Submission Guidelines.

⁵⁷ New York City Administration for Children's Services: Research Proposal Submission Guidelines.

⁵⁸ In 2017, OHRP determined that although pregnant women are entitled to additional protections under 45 CFR Part 46 Subpart B, they should not be considered a population that is "vulnerable to coercion or undue influence" due solely to their pregnancy status. *See* 82 Fed. Reg. 7203-7204 (Jan. 19, 2017) ("In agreement with the majority of comments, the final rule no longer includes pregnant women...as examples of populations that are potentially vulnerable to coercion or undue influence.")

⁵⁹ 45 C.F.R. §§ 46.201-46.207.

⁶⁰ 45 C.F.R. §§ 46.305 and 46.306.

⁶¹ https://humansubjects.nih.gov/prisoners_categories_research.

⁶² New York State Task Force on Life and the Law, *Report and Recommendations For Research With Human Subjects Who Lack Consent Capacity*, (January 2014), https://www.health.ny.gov/regulations/task_force/docs/report_human_subjects_research.pdf.

⁶³ NIH, *Research Involving Individuals with Questionable Capacity to Consent: Points to Consider*, (November 2009), available at <http://grants1.nih.gov/grants/policy/questionablecapacity.htm>; OHRP: Institutional Review Board Guidebook, Chapter VI, Section D, *Cognitively Impaired Persons*, available at http://wayback.archive-it.org/org-745/20150930182815/http://www.hhs.gov/ohrp/archive/irb/irb_chapter6.htm ; New York State Task Force on Life and the Law, *Report and Recommendations For Research With Human Subjects Who Lack Consent Capacity*, (January 2014), https://www.health.ny.gov/regulations/task_force/docs/report_human_subjects_research.pdf.

⁶⁴ New York Public Health Law §2994-d(1).

⁶⁵ NYS Public Health Law § 2444(2).

⁶⁶ N.Y. Mental Hyg. Law § 33.13(c)(9)(iii).

⁶⁷ 14 NYCRR § 815.11.

⁶⁸ N.Y. Mental Hyg. Law § 22.05(a). See also 42 C.F.R. § 2.52 regarding the disclosure of patient identifying information in the course of Research.

⁶⁹ 42 C.F.R. § 2.52(b).

⁷⁰ 42 C.F.R. § 2.52(c).

⁷¹ 20 U.S.C. § 1232g; 34 C.F.R. Part 99.

⁷² 20 U.S.C. § 1232h; 34 C.F.R. Part 98.

⁷³ 20 U.S.C. § 1232g(b).

⁷⁴ 20 U.S.C. § 1232h(a).

⁷⁵ 20 U.S.C. § 1232h(b).

⁷⁶ http://schools.nyc.gov/NR/rdonlyres/F1942EF6-CE3D-4A8D-AE56-6B709EC70265/0/Proposal_Guidelines_Revised2102012.pdf.

⁷⁷ 45 C.F.R. § 46.111(b).

⁷⁸ 42 U.S.C. § 241(d)(1).

⁷⁹ *Notice of Changes to NIH Policy for Issuing Certificates of Confidentiality*, available at <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html>.

⁸⁰ 42 U.S.C. § 241(d)(1)(B).

⁸¹ 42 U.S.C. § 241(d)(1)(C).

⁸² 42 U.S.C. § 241(d)(1)(A). See also *Notice of Changes to NIH Policy for Issuing Certificates of Confidentiality*, available at <https://humansubjects.nih.gov/coc/faqs>.

⁸³ 42 U.S.C. § 241(d)(4). See also *NIH Frequently Asked Questions, Certificates of Confidentiality*, Section A.6, available at <https://humansubjects.nih.gov/coc/faqs>.

⁸⁴ *Notice of Changes to NIH Policy for Issuing Certificates of Confidentiality*, available at <https://humansubjects.nih.gov/coc/faqs>.

⁸⁵ *NIH Frequently Asked Questions, Certificates of Confidentiality*, Section B.4, available at <https://humansubjects.nih.gov/coc/faqs>.

⁸⁶ *NIH Frequently Asked Questions, Certificates of Confidentiality*, Section C.1, available at <https://humansubjects.nih.gov/coc/faqs>.

⁸⁷ *NIH Frequently Asked Questions, Certificates of Confidentiality*, Section E, available at <https://humansubjects.nih.gov/coc/faqs>.

⁸⁸ 81 Fed. Reg. 183, 64982 (Sept. 21, 2016); 42 CFR Part 11; NIH Policy on Dissemination of NIH-Funded Clinical Trial Information, available at <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-149.html>. The NIH defines clinical trial to mean “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 those interventions on health-related biomedical or behavioral outcomes.”

⁸⁹ OHRP Guidance on Withdrawal of Subjects from: Data Retention and Other Related Issues, available at <http://www.hhs.gov/ohrp/policy/subjectwithdrawal.html>.

⁹⁰ 21 C.F.R. § 312; *Investigational New Drug Applications Prepared and Submitted by Sponsor-Investigators: Guidance for Industry*, available at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM446695.pdf>.

⁹¹ 21 C.F.R. § 312.2.

⁹² 21 CFR §§ 312.60, 312.61, 312.62, 312.64, 312.66, 312.68.

⁹³ *See Device Advice: Investigational Device Exemption*, available at <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/default.htm>.

⁹⁴ 21 C.F.R. Part 50; 21 C.F.R. Part 56; 21 C.F.R. 812.

⁹⁵ 21 C.F.R. § 812.2(c).

⁹⁶ 21 C.F.R. § 812.2(b).

⁹⁷ 21 C.F.R. § 812.42.

⁹⁸ 21 C.F.R. 812.66.

⁹⁹ 21 C.F.R. § 812.100; 21 C.F.R. § 812.110.

¹⁰⁰ 21 C.F.R. § 812.100, Subpart H.

¹⁰¹ 21 C.F.R. § 814.100.

¹⁰² 21 C.F.R. § 814.124.

¹⁰³ 21 C.F.R. § 312.300.

¹⁰⁴ *See* FDA guidance documents *Expanded Access (Compassionate Use)*, available at <https://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm>; *Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers: Guidance for Industry*, available at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM351261.pdf>.

¹⁰⁵ *Individual Patient Expanded Access Applications: Form FDA 3926 – Guidance for Industry*, Section B.III, available at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM432717.pdf>.

¹⁰⁶ 21 C.F.R. § 312.310.

¹⁰⁷ 21 C.F.R. § 312.305(d).

¹⁰⁸ 21 C.F.R. § 312.305(c)(4); *Expanded Access for Investigational Drugs for Treatment Use – Guidance for Industry*, Section Q6, available at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM351261.pdf>).

¹⁰⁹ 21 CFR § 312.305(c)(4).

¹¹⁰ *Expanded Access for Medical Devices*, available at <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm#compassionate>.

¹¹¹ *Expanded Access for Medical Devices*, available at <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm#compassionate>.

¹¹² 21 C.F.R. § 812.36(d).

¹¹³ 21 C.F.R. § 56.104(c).

¹¹⁴ FDA requirements for legally effective informed consent are outlined at 21 C.F.R. §§ 50.20, 50.25, and 50.27.

¹¹⁵ 21 CFR § 50.23.

¹¹⁶ 21 C.F.R. § 312.310(d)(2); *Expanded Access for Investigational Drugs*, available at <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM351261.pdf>.

¹¹⁷ 42 U.S.C. Section 262.

¹¹⁸ GCP Guidance, Sections 7.1 and 7.3.

¹¹⁹ GCP Guidance, Section 5.18; 21 C.F.R. § 312.53(d).

¹²⁰ 21 C.F.R. § 312.53(b); GCP Guidance, Section 5.14.

¹²¹ GCP Guidance, Section 4.6.2.

¹²² GCP Guidance, Section 4.2.3.

¹²³ GCP Guidance, Section 4.2.4; 10 NYCRR 405.17(a)(9).

¹²⁴ GCP Guidance, Section 4.6.3; N.Y. Edu. Law § 6817(1)(a).

¹²⁵ 21 C.F.R. § 312.62.

¹²⁶ 10 NYCRR 405.17(a)(6).

- ¹²⁷ 21 C.F.R. § 312.53(b).
- ¹²⁸ 10 NYCRR § 405.17(c)(2).
- ¹²⁹ 21 C.F.R. Part 11.
- ¹³⁰ 21 C.F.R. § 312.6(a).
- ¹³¹ <http://www.usp.org/usp-healthcare-professionals/compounding/compounding-general-chapters>.
- ¹³² 21 C.F.R. § 312.59.
- ¹³³ 10 NYCRR 405.17(b)(4).
- ¹³⁴ N.Y. Civ. Rights Law § 79-L (2)(b)(7).
- ¹³⁵ N.Y. Civ. Rights Law § 79-L (2)(f).
- ¹³⁶ N.Y. Civ. Rights Law § 79-l(2)(b); Wadsworth Genetic Testing Standard 5, available at https://www.wadsworth.org/sites/default/files/WebDoc/1184889505/GETE_June2014.pdf.
- ¹³⁷ N.Y. Civ. Rights Law § 79-L (2)(f).
- ¹³⁸ N.Y. Civ. Rights Law § 79-l(4)(a).
- ¹³⁹ N.Y. Civ. Rights Law § 79-l (2)(c) and (9)(a); Wadsworth Genetic Testing Standard 1, available at https://www.wadsworth.org/sites/default/files/WebDoc/1184889505/GETE_June2014.pdf.
- ¹⁴⁰ N.Y. Civ. Rights Law § 79-l (9)(e).
- ¹⁴¹ N.Y. Civ. Rights Law § 79l(9)(b).
- ¹⁴² N.Y. Civ. Rights Law § 79-l(9)(c).
- ¹⁴³ The Genetic Information Nondiscrimination Act, 42 U.S.C., Chapter 21F.
- ¹⁴⁴ OHRP Guidance on the Genetic Information Nondiscrimination Act: Implications for Investigators and Institutional Review Boards, available at <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-genetic-information-nondiscrimination-act/index.html>.
- ¹⁴⁵ N.Y. Civ. Rights Law § 79-1(3)(a) and (b), and (9)(d); Wadsworth Genetic Testing Standard 14, available at https://www.wadsworth.org/sites/default/files/WebDoc/1184889505/GETE_June2014.pdf.
- ¹⁴⁶ OHRP Guidance on the Genetic Information Nondiscrimination Act: Implications for Investigators and Institutional Review Boards, available at <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-genetic-information-nondiscrimination-act/index.html>.
- ¹⁴⁷ N.Y. Civ. Rights Law § 79-l(11); see also N.Y. Pub. Health Law § 4302-4309 with regard to anatomical gifts and terms of use.
- ¹⁴⁸ 67 Fed. Reg. 53182, 53231.

¹⁴⁹ N.Y. Civ. Rights Law § 79-l(9)(b).

¹⁵⁰ N.Y. Civ. Rights Law § 79-l(10).

¹⁵¹ N.Y. Pub. Health Law § 4300, *et seq.*

¹⁵² N.Y. Pub. Health Law §§ 4302, 4303.

¹⁵³ 42 C.F.R. §§ 93.309, 93.310(b).

¹⁵⁴ The term “protocol deviation” is not defined by either the HHS human subject regulations (45 C.F.R. Part 46) or the FDA human subject regulations (21 C.F.R. Part 50).

¹⁵⁵ See <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm126572.pdf>.

¹⁵⁶ 45 C.F.R. § 46.108(a)(3)(iii).

¹⁵⁷ 45 C.F.R. § 46.108(a)(3)(iii).

¹⁵⁸ There are many acceptable definitions for Adverse Events. H+H has adopted the above definition to be used as a default if no other definition is documented in any given Research Protocol. Research Project teams with a commercial Sponsor should always follow the definitions outlined in their Sponsor’s Research Protocol, unless the definition of Adverse Event is less stringent than the definition provided above, in which case the definition provided in this policy should be used. If the Research Protocol is an H+H Principal Investigator initiated protocol, the above definition should be utilized.

¹⁵⁹ 45 C.F.R. § 46.108(a)(4)(i).

¹⁶⁰ 45 C.F.R. § 46.108(a)(4)(i).

¹⁶¹ 10 NYCRR § 404.10(b); Section 482.24(c) STATE OPERATIONS MANUAL, Appendix A-Survey Protocol, Regulations and Interpretive Guidelines for Hospitals.

¹⁶² See, e.g. 21 CFR § 312.62 and 21 CFR 812.140.

¹⁶³ N.Y. Arts & Cult. Aff. Law § 57.25; 8 NYCRR § 185.5; New York State Archives *Records Retention and Disposition Schedule MI-1*, at 132, available at http://www.archives.nysed.gov/a/records/mr_pub_mi1_part1.shtml; 8 NYCRR § 29.2; see also 45 CFR § 164.528 (accounting for disclosures of identifiable health information made in the context of research).

¹⁶⁴ 45 C.F.R. 46.115(b).

¹⁶⁵ 45 C.F.R. Part 46.

¹⁶⁶ 8 NYCRR Part 185.

¹⁶⁷ 45 C.F.R. § 46.116(a)(6), 21 C.F.R. § 50.25(a)(6).

¹⁶⁸ Medicare National Coverage determinations Manual 310.1 (Routine Costs in Clinical Trials) as modified by Medicare Coverage Decision Memorandum for the Clinical Trial Policy dated July 9, 2007.

¹⁶⁹ 45 C.F.R. § 75.403.

¹⁷⁰ 45 C.F.R. § 75.405.

¹⁷¹ 45 C.F.R. § 75.404.

¹⁷² NIH Grants Policy Statement, October 1, 2017, Section 19.2, Definitions.

¹⁷³ NIH Grants Policy Statement, October 1, 2017, Section 19.3, Policy.

¹⁷⁴ Centers for Medicare and Medicaid Services National Coverage Decision for Routine Costs of a Clinical Trial, July 9, 2007.

¹⁷⁵ NIH Grants Policy Statement, October 1, 2017, Section 19.2, Definitions.

¹⁷⁶ NIH Grants Policy Statement, October 1, 2017.

¹⁷⁷ Medicare National Coverage Determinations Manual Section 310.1.

¹⁷⁸ Draft Office of Inspector General Compliance Program Guidance for Recipients of Public Health Service Awards, 70 Fed. Reg. 71312 (Nov. 28, 2005), at section II.B; 2 CFR §§ 200.302(b)(4).