

OPERATING PROCEDURE NO.: 180-9

**HHC 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: Ram Raju, MD

DATE: April 29, 2015

RE: HHC Human Subject Research Protections Program Policies and Procedures

This Operating Procedure, **HHC Human Subject Research Protections Program Policies and Procedures** replaces the **HHC Clinical Investigation and Research Policy and Guidelines** dated May 23, 1991.

SCOPE: This Operating Procedure applies to all individuals involved with Research conducted at HHC facilities.

EFFECTIVE DATE: Immediately

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PREAMBLE

I. MISSION

HHC supports and promotes Research through fostering academic-community partnerships in which 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 HHC institutions to promote and protect health in its fullest sense; the total physical, mental and social well-being of the people.

HHC 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. HHC will assist investigators to be properly trained to develop and conduct research and will facilitate the appropriate conduct of Research. HHC will also work with its 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 HHC Human Subject Research Protections Program Policies and Procedures ("Policies and Procedures") is to provide guidance to members of the Research Team in complying with the ethical standards described in the Belmont Report and applicable federal, state and local laws and regulations that govern Research carried out, in whole or in part, at any of the facilities of the New York City Health and Hospitals Corporation (hereafter "HHC"). For clarification, the term "Research" includes research which uses HHC patients, facilities, staff or resources or which is conducted at an HHC facility; it only includes human research, (i.e. not animal studies). In order to protect Human Subjects and guide researchers, all individuals involved in Research at HHC 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.

III. SCOPE

A. To Whom These Policies and Procedures Apply. These Policies and Procedures apply to all individuals involved with Research conducted at HHC Facilities.

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 HHC, 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 HHC 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 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 HHC's commitment to detecting and deterring criminal conduct, fraud, waste and abuse in Human Subject Research is fulfilled.¹

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 the U.S. Department of Health and Human Services (DHHS), HHC 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 Federalwide Assurance (FWA).

HHC'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), and all applicable federal policies.

HHC will ensure that IRBs designated under HHC's FWA are approved by the New York State Department of Health, to the extent required by law, and registered with OHRP² as well as the FDA where the IRB reviews clinical investigations regulated by the FDA.³ Further, HHC will ensure that, where any responsibilities are delegated to an IRB, an IRB Authorization Agreement is executed between HHC and the IRB. In addition, a current copy of HHC'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 RA Office 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.

HHC is committed to conducting research with the highest regard for the welfare of human participants. It upholds, and adheres to, the principles of The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research by the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research (1979)⁴ ("Belmont Report").

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

HHC 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

A. Other HHC Operating Procedures Superseded by these Policies and Procedures

These Policies and Procedures supersede HHC Operating Procedures 160-001: HHC Review, Approval and Cost Recovery from Affiliation-Sponsored Research Activities Performed in Corporation Facilities; HHC Operating Procedure 140-004: Receipt, Storage, Dispensing and Accountability of Investigational New Drugs; the 1991 Board Policy entitled “HHC Clinical Investigation & Research Policy & Guidelines”; and any and all individual Facility policies related to Research; HHC Operating Procedure 40-6: Grants, Trust, Donations, to the extent monies are given to HHC for Research and also to the extent any donations are of anatomical gifts.

B. Other HHC Operating Procedures Not Superseded by these Policies and Procedures

These Policies and Procedures do not supersede HHC Operating Procedure 240-23: HIPAA Clinical Investigation and Research Policy and Guidelines; HHC Operating Procedure 40-59: Time and Effort Reporting and Operating Procedure; HHC Operating Procedure 40-6: Grants, Trust, Donations, except to the extent monies are given to HHC 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

HHC 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 HHC, unless any memorandum of understanding or other agreement between HHC and the Grantee directs otherwise. The policies and procedures of HHC 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 PI should seek from the Office of Research Administration written guidance with respect to his or her obligations under those conflicting policies and procedures.

VI. ROLES & RESPONSIBLE PARTIES

A. HHC'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 HHC patients involved in research at its Facilities; and
3. providing access to an Institutional Review Board ("IRB") that will approve any proposed Research by either providing such IRB internally or contracting with an external IRB. HHC 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 New York State Department of Health to the extent required by law.

B. HHC'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 PI, 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 HHC Office of Research Administration.

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

1. The goals of the Research Council are:
 - a. to foster and strengthen internal and external partnerships and scientific collaborations to enable HHC 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 HHC's mission;
 - c. to promote systems thinking approach to identify existing barriers to research within HHC 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 HHC Chief Medical Officer and work closely with the HHC 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 HHC. 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 HHC Facilities, as well as Central Office.
- d. monitor HHC's progress towards implementing HHC's research agenda, monitor strengths, weaknesses and risks, and recommend resolution strategies.
- e. work with and review HHC 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 HHC regarding updates.
- g. provide leadership in supporting novel science and safe application of scientific discoveries to the community.

D. The Chief Medical Officer of HHC has been appointed as the Signatory Official under HHC'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.⁵
3. reporting to the HHC Board of Directors and/or the Quality Assurance Committee of the Board periodically regarding human research protection activities, audit results, investigations, findings, and other information with respect to identified risk areas.
4. In addition, the Chief Medical Officer is responsible for reporting to the HHC Board of Directors and HHC executive leadership on an annual basis the

summary of Research performed at HHC compiled by the RA Office described in paragraph VI.F.4 of this Preamble.

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

1. serving under the FWA as the point of contact with United States Department of Health and Human Services Office of Human Research Protections 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 HHC fulfills its responsibilities under its FWA;
3. setting standards for Human Subject Research education requirements;
4. ensuring that all HHC personnel overseeing Research at HHC participate in and complete regular training with respect to human subject research protections;
5. ensuring that all IRBs utilized by HHC have entered into an IRB Authorization Agreement with HHC 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 RA Office’s oversight activities with respect to compliance with these Policies and Procedures.

F. The Office of Research Administration (the “RA Office”) works in concert with the HHC 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 HHC research community. In addition, the RA Office has the following responsibilities:

1. *Education.* Leading educational efforts for PIs and their staff, researchers and research staff, and appropriate corporate officials, to:
 - a. Review, recommend and approve CITI 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. Providing counseling to PIs, researchers and all others as requested and needed.
 - b. Visiting facilities regularly and meeting with FRC, FRRC, PIs, research staff and grants officers.
3. *Compliance and Oversight.*
- a. Overseeing the compliance of any ongoing Research involving Human Subjects with Federal, State and Corporate regulations and report any problems or concerns to the HHC Office of Legal Affairs, Office of Corporate Compliance, and Facility Executive Directors and/or Medical Directors, Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP), as required.
 - b. Overseeing HHC compliance with Federal and State regulations regarding protection of human subjects and report any problems or concerns to the HHC Office of Legal Affairs, Office of Corporate Compliance, and Facility Executive Directors and/or Medical Directors, and OHRP, as required.
 - c. Researching and selecting IRBs for HHC; and reviewing the IRB Policies and Procedures for compliance with federal and state requirements.
4. *Reporting to HHC Board of Directors and Corporate Leadership.* The RA Office will be responsible for compiling a summary of the scope and type of Research performed at HHC to be presented to the HHC Board of Directors and executive leadership on an annual basis.

G. The Principal Investigator (“PI”) 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 HHC and the overall conduct of the project. The PI 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. This individual 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 PI may delegate Research Project-related tasks, but must adequately supervise Research personnel to whom tasks are delegated. When supervising the conduct of Research, the PI 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 PI 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 PI should attempt to inform the Human Subject's primary care physician, if medically appropriate, about the 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 PI's (or his/her delegate's) responsibilities include obtaining valid Informed Consents prior to commencing Research;⁶ adhering to IRB requirements with respect to progress reports, continuing review and approvals; reporting to the IRB any unanticipated problems involving risks to subjects or others;⁷ 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, HHC and sponsor close-out procedures upon completion of the Research Project; and, if requested, making Research records available to HHC, 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 Rule⁸ and other federal laws and regulations, applicable state and local law governing the conduct of research, HHC 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 HHC policies and procedures and relevant law governing research, seek advice from the RA Office, FRC, PI, IRB or Sponsor or Grantor, as applicable; and

3. must complete any educational training required by HHC, 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 and 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 HHC 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.⁹ 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 RA Office will make such determinations centrally, in consultation with the Office of Legal Affairs, CMO, PI, Office of Corporate Compliance and the FRC as needed. The RA Office will communicate such determinations to the applicable IRB, all Principal Investigators, and related research staff.

B. Compliance with Law, Regulations and Policies

HHC shall ensure that all Research is conducted in compliance with applicable Federal, New York State and local laws, 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 HHC staff.

IX. EFFECTIVE DATE

These Policies and Procedures are effective as of _____, 2014.

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 HHC has entered into an agreement which contemplates a relationship and/or involves research activities or patient care.

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

“**Chief Nurse Executive**” means the chief nursing officer of HHC.

“**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 HHC.

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

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

“**FRC**” means the Facility Research Coordinator who is appointed by the Executive Director of the Facility.

“**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 HHC by the Federal or State Government for a specific purpose to support instruction, research, or health or other public service.

“**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.

“**HHC**” means the New York City Health and Hospitals Corporation.

“**Human Protections Administrator**” means the Director of the HHC Office of Research Administration.

“Human Subject” means an individual that meets the definition of Human Subject under 45 C.F.R. Part 46¹⁰ or 21 C.F.R. §50.3(c)¹¹ or New York Public Health Law Article 24-A,¹² regardless of whether direct patient care services are rendered to such individual. This term includes an individual whose tissue is used in Research and who may be individually identifiable by a PI or the PI’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 and 21 C.F.R. 50.25.¹³

“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 HHC 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” or **“OLA”** means to Office of Legal Affairs of HHC.

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

“Principal Investigator” or **“PI”** means the individual who i) is qualified under 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 RA Office.

“RA Office” means the HHC Office of Research Administration.

“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 HHC patients, facilities, staff or resources or which is conducted at a Facility.

“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 HHC HIPAA Clinical Investigation and Research Policy and Guidelines, at Section 2.1.

“Research Council” means the body of HHC Facility representatives that serves as an expert advisory committee to HHC 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 Protocol” means the written description of the scope of work to be performed in the performance of the Research Project and which is submitted to the IRB for 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 HHC

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 and/or other clinical staff, as outlined below:

1.1.1. Physicians. A physician may act as PI 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, clinical staff may act as PI 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.¹⁵

1.1.3. Students. Students 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 PI 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. TRAINING OF RESEARCH TEAM, REVIEWERS AND OTHERS.

2.1. **Policy.**

Federal 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 HHC ethical standards, HHC 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 subjects protections.

2.2. **Procedure.**

2.2.1. **Research Team Training.**

(a) *Initial training.* Prior to their involvement in human subject research and before commencing Research at HHC 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 RA Office, 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 two years. Continuing education requirements may be met either by completing a CITI refresher course or other training required by the RA Office.

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

2.2.2. **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, as determined by the RA Office.

2.2.3. **Training for Other Research Personnel.** Others who are involved in the review of Research at HHC, such as the Facility Research Coordinator and Facility Executive Directors, must participate in and complete selected modules of training offered by

the DHHS's National Institute of Health, as determined and deemed necessary by the RA Office.

2.2.4. Education Tracking. The RA Office is responsible for tracking fulfillment of training requirements. As such, the RA Office will have access to the online record of training completion reports and may also maintain local records of completion dates.

SECTION 3. HHC RESEARCH APPROVAL PROCESS

3.1. Policy

In order to ensure that researchers comply with Federal, State, City and Corporate policies and regulations that guide human subjects research at HHC, all Research Projects must undergo the approval process described herein.

HHC 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 HHC executive officers and lastly, the HHC RA Office.

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

3.2. Procedures

3.2.1. STEP I: Pre-Approval of the Research Project. This phase is to determine a Research Project's operational and financial practicability at HHC. 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 PI should 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. The FRC can involve as many expert reviewers as needed, and the PI may request that the Facility's Executive Director or Medical Director be included in the feasibility review.

(a) *Multi-Facility Research Projects*. Where a PI intends to conduct Research at multiple HHC Facilities, the PI should contact the RA Office to facilitate pre-approval. In addition, a Facility, PI or other contact person should be identified for each Facility engaged in the Research Project.

(b) *Collaborative Research Projects*. If any Research Project is to be undertaken with an Affiliate, the PI should also consult with the appropriate offices within the Affiliate if required by such Affiliate's policies regarding collaborative research.

3.2.2. STEP II: IRB and Facility Review and Approval, and Contract/Agreement Negotiations.

(a) *IRB Submission.* 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 subject. (Please see Section 4 of these Policies and Procedures regarding Informed Consent, and HHC 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 PI.

(c) *Facility Review and Approval Process.*

(i) *STAR.* In order to obtain final Facility approval, the PI must submit an application for the Research Project by uploading required information with respect to the IRB determination directly into the electronic submission system, which is the System to Track and Approve Research (STAR). Facility reviews should be confined to ascertaining the completeness of the submission; it is not to 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 PI and work with the PI for appropriate action. A completed application will include:

- (1) the Research Protocol, the IRB determination letter,
- (2) any Informed Consent/waivers/alterations, and HIPAA Research Authorization Form and/or waivers thereof,
- (3) any applicable contract with the Grantor or Sponsor, if executed; and
- (4) any applicable approved budget or billing plan in accordance with Section 29.3 or coverage analysis, if applicable under Section 31.3.2 for the Research Project.

(iii) *FRRC Review of the Completed Application.* The FRRC will review the completed application made through STAR in a timely manner. If the FRRC cannot approve the Research Project as submitted

by the PI, it will promptly communicate such findings to the PI. (Please see HHC 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 HHC and the Affiliate describes how Research Project Costs (as that term is defined in Section 29.1) are to be calculated and paid to HHC, the FRRC may not approve the proposed Research Project until HHC and Affiliate have agreed in writing how such costs will be reimbursed to HHC with respect to such proposed Research Project and such agreement has been approved by the OLA.

(iv) Facility Executive Review and Approval. If the FRRC approves a Research Project, the completed application should be submitted 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, the application should be sent directly to the RA Office.

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 PI, who may then discuss the decision with the Executive Director. If the PI and Executive Director cannot reach an agreement, the PI 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.

(d) Contract/Agreement Negotiations.

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

(ii) Once the RA Office has finalized the contract, it will be forwarded to OLA for final review and approval. The RA Office will notify the PI and FRC once the contract has been approved and provide a copy of the final contract to the PI.

(iii) The CMO is authorized and is required to sign on behalf of HHC all Research agreements with a Sponsor or Grantor that have been reviewed by the RA Office and approved by OLA as set forth above.

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

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

3.2.3. STEP III: RA Office Review and Approval.

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

(b) *RA Office Review.* The application sent to the RA Office for review must be complete and accurate. The RA Office 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 RA Office 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 HHC 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 RA Office.

(c) *HHC Approval Communicated to PI.* The RA Office, via STAR, will promptly notify the PI, 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, one HHC approval letter will be generated per Facility.

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

3.2.5. *Modifications.* If PIs 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 RA Office.

SECTION 4. INFORMED CONSENT

4.1. **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 HHC 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, FDA and New York State regulations.¹⁶

4.2. **Procedure.**

4.2.1. **Elements of Consent**

(a) *Basic Elements of Consent*

Informed consent documents or other methods used to obtain consent must include the basic requirements of DHHS¹⁷ and FDA regulations¹⁸ (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 § 79-1 with regard to research involving genetic testing (see Section 19 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 which 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 which 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.") For research involving more than minimal risk,¹⁹ 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;

(vi) 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; and

(vii) 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.

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

(i) When appropriate, the federal regulations indicate that one or more of the following elements of information shall be provided to each Human Subject:

(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) which are currently unforeseeable;

(2) Anticipated circumstances under which the Human Subject's participation may be terminated by the investigator without regard to the Human Subject'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 which may relate to the Human Subject's willingness to continue participation will be provided to the Human Subject; or

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

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

(1) A provision for the Human Subject or his or her legally authorized representative, as applicable, to be given a copy of the consent form, if the consent is written;

(2) Identification of the sponsor in sponsor-initiated Research Projects;

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

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

(5) 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;

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

(7) 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

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

(c) *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:

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

(ii) 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;

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

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

(v) 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

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

(d) *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.”

4.2.2. Waiver of Consent Requirements

(a) *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 the following:

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

(1) The Research is not FDA-regulated;

(2) The Research involves no more than minimal risk to the Human Subjects;

(3) The waiver or alteration will not adversely affect the rights and welfare of the Human Subjects;

(4) The Research could not practicably be carried out without the waiver or alteration; and

(5) Whenever appropriate, the Human Subjects will be provided with additional pertinent information after participation.

(ii) Government conducted or approved studies.

(1) The Research is not FDA-regulated;

(2) 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

(3) 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 4 (Emergency Use of an Investigational Drug or Device) of these Policies and Procedures.

4.2.3. Documenting Consent

(a) *Generally.* In general, Informed Consent must be documented unless the IRB has determined that it can be waived under DHHS 45 C.F.R. § 46.117(6) 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) The consent signature(s) should be obtained as follows:
 - (1) The Human Subject or the Human Subject's legally authorized representative must be asked to sign and date the consent document.
 - (2) The person obtaining the Human Subject's consent must sign and date the document, if required by the Research Project protocol, the IRB, or Research Project sponsor.
 - (3) A witness to the Human Subject's signature must sign and date the document, if required by the Research Project protocol, the IRB, or Research Project sponsor.
 - (4) In all cases, signatures on the consent document may only be dated by the individuals who sign the document.

(ii) The Human Subject or the Human Subject's legally authorized representative will be given a copy of the consent document unless waived per DHHS 45 C.F.R. § 46.117(c) or FDA 21 C.F.R. § 50.27.

(b) *Waiver of Informed Consent*

(i) Federal regulations²⁰ permit the IRB to approve a consent procedure which does not include, or which alters, some or all of the elements of Informed Consent set forth in this section, or waive the requirements to obtain Informed Consent provided the IRB finds and documents that:

(1) the Research Project involves no more than minimal risks to Human Subjects;

(2) the waiver or alteration will not adversely affect the rights and welfare of the Human Subjects;

(3) the Research Project could not practicably be carried out without the waiver or alteration; and

(4) whenever appropriate, the Human Subjects will be provided with additional pertinent information after participation.

(ii) A waiver of Informed Consent may also be approved on certain research and demonstration projects designed to study public benefit or service programs as specified in the regulations.

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

(i) The IRB is also permitted by federal regulations²¹ 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 consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the Human Subject 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.

(ii) In cases in which the documentation requirement is waived, the IRB may require the PI to provide Human Subjects with a written statement regarding the Research Project.

(d) *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.

4.2.4. 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 subject or the representative is made to waive or appear to waive any of the subject's legal rights or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence. 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:

HHC 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.

4.2.5. 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.

4.2.6. 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. PIs are encouraged to contact the applicable IRB for these forms.

4.2.7. Sponsor-Prepared Consent Documents. While PIs 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.

4.2.8. 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.

4.2.9. 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.

4.2.10. 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 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 investigator on how to proceed. Measures should be taken to prevent future omissions of the signature date.

4.2.11. 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 5. EMERGENCY USE OF AN INVESTIGATIONAL DRUG OR DEVICE

5.1. **Definitions:**

For purposes of this Section 4, the following definitions shall apply.

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

“**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.

“**Investigational Drugs**” means 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.

“**Life-threatening**” refers to diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the Recipient must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.

“**Severely debilitating**” means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

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

5.2. **Policy**

HHC permits emergency use of an unapproved device, drug or biologic intended to benefit a single Human Subject who is not enrolled in or eligible for a Research Project, provided the requirements of this Section are met. HHC requires consultation with the IRB and the RA Office prior to use, if practicable.

Generally, emergency use of a Test Article requires either an emergency IND²² (for Investigational Drugs) or an Investigational Device Exemption (for Investigational Devices).²³ FDA regulations provide an “emergency use” exemption from rules requiring prior IRB review and approval.²⁴ Research designed to evaluate emergency care treatments is not “emergency use.” As with all other Research, prospective IRB review and approval are required before a Research Project in emergency medicine can commence. The exception from Informed Consent for these Research Projects is provided by federal regulations enforced by the U.S. Food and Drug Administration²⁵ and Office of Human Research Protections.²⁶

The FDA and DHHS regulations differ in that under FDA regulations, an emergency use of an Investigational Drug or Investigational Device constitutes a “clinical investigation” while DHHS regulations do not contemplate an instance of emergency use of an Investigational Drug or Investigational Device as “research” because neither the Human Subject nor the Research Project Data will be part of a systematic investigation designed to develop or contribute to generalizable knowledge. Therefore, emergency use is not subject to DHHS regulations under 45 C.F.R. Part 46. However, reporting the use to the IRB is required by the FDA.

5.3. **Procedures**

5.3.1. **General Requirements.**

(a) *Prior to the Emergency Use.*

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

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

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

(iv) 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.

(v) 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.

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

(vii) 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. PIs will send a copy of the report to the RA Office in a timely manner.

(viii) PIs are responsible for ensuring that the recipient is not included in a systematic investigation designed to develop or contribute to generalizable knowledge.

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

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

(3) 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 HHC Office of Legal Affairs to ascertain whether this constitutes Research requiring IRB and HHC review and approval.

(b) *After the Emergency Use.*

(i) 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.

(ii) 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 HHC, and, if necessary, work with the department chair and RA Office to initiate efforts to obtain approval from HHC, the appropriate IRB, and regulatory clearance from the FDA to allow for the broadest possible future use of the drug.

5.3.2. Specific Requirements for the Emergency Use of Investigational Drugs.

(a) *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.

Emergency use of an Investigational Drug requires an exemption from the approved use of the Investigational Drug. This may be accomplished in one of three ways:

(i) 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.

(ii) 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.

(iii) If the use may not occur under an existing IND, but the IND holder is willing to provide the Test Article, the PI 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.

(b) *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 5.3.5.

5.3.3. Specific Requirements for the Emergency Use of Investigational Devices. In the event that the PI determines that an emergency use of an Investigational Device is needed, the PI must contact the IRB and should consult with the RA Office for guidance with respect to such emergency use.

5.3.4. Informed Consent for Emergency Use of a Test Article. The PI must obtain the Informed Consent of the prospective recipient or a legally authorized representative, or else determine that the emergency use meets the criteria for an exception to the requirement for Informed Consent, as detailed below.

(a) Except as outlined below, Principal Investigators are required to obtain legally effective Informed Consent for the emergency use of a Test Article.²⁷

(b) FDA regulations²⁸ provide for an exception from general requirements for Informed Consent if the Principal Investigator and a physician not otherwise involved in the emergency use, certify in writing that all of the following criteria are met:

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

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

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

(iv) 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.

5.3.5. Second Use of a Test Article.

(a) In cases where a Test Article has previously been used in an emergency at HHC, 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:

(i) The Facility's medical director or designee must determine that although the Test Article has been used at HHC in a previous emergency, there is insufficient time to obtain IRB review and approval for the second emergency use.

(ii) The determination must also include justification for the additional use.

(iii) The determination must be made prior to emergency use.

(b) 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.

SECTION 6. RESEARCH INVOLVING RECOMBINANT DNA

6.1. Definitions:

For purposes of this Section 8, the following definitions shall apply:

“Human gene transfer” means the deliberate transfer into human research participants 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.

“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.²⁹

6.2. **Policy:**

HHC is responsible for ensuring that all research involving Human Subjects and recombinant or synthetic nucleic acid molecules and human gene transfer conducted at HHC is conducted in compliance with the NIH Guidelines for Research Involving Recombinant DNA Molecules³⁰ (the “NIH Guidelines”), the CDC guidelines on Biosafety in Microbiology and Biomedical Laboratories,³¹ 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. HHC’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.³² HHC is also responsible for ensuring adequate expertise and training,³³ and filing an annual report with the Office of Biotechnology Activities (OBA).³⁴ In addition, HHC is responsible for obtaining NYSDOH approval for any Research Project involving recombinant DNA.³⁵

6.3. **Procedure:**

6.3.1. *Research Proposals and Protocols*

- (a) In addition to the Research Approval Process set forth in Section 3 of these Policies and Procedures, the PI 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 HHC to the applicable IBC for review and approval in accordance with the IBC’s submission requirements.³⁶

(b) PIs involved in human gene transfer Research are required to obtain additional approvals from the NIH³⁷ 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,'³⁸ which includes adverse event/safety reporting requirements for those PIs who have received approval from the FDA to initiate a human gene transfer protocol. PIs involved in such protocols must report 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 HHC's Research Approval Process. In turn, HHC may not approve the conduct of a Research Project involving recombinant or synthetic nucleic acid molecules that has been disapproved by the relevant IBC.

6.3.2. *PI Responsibilities After Recombinant DNA Research Approval.*

Once the PI has received both IBC and HHC approval to conduct Human Subject Research involving recombinant or synthetic nucleic acid molecules, the Principal Investigator shall have the following responsibilities:³⁹

- (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/OBA, the RA Office, FRRC, and other appropriate HHC 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

HHC recognizes the need to protect vulnerable populations. Consequently, when assembling the application to be submitted to the IRB and approval submissions discussed in Section 3 and Section 12 (Research Approval Process and Renewal of Research Approval, respectively), the Principal Investigator should be mindful of vulnerable classes of Human Subjects and the regulatory requirements that must be met before an IRB can approve a protocol or proposed consent form. These classes include children, prisoners, pregnant women, fetuses & neonates and decisionally-impaired adults. In addition to the above groups of vulnerable populations, there are several populations that should also be given special consideration and may require additional safeguards. These groups include, but are not limited to students in schools or 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.⁴⁰

(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.⁴¹ Regardless of the level of risk involved, the PI 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. §§ 46.117, and 46.405 through 46.408.⁴² 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 abuse services, and sexual assault treatment.

(c) The FRRC or the RA Office in their respective reviews during the Research Approval Process (Section 3) and Renewal of Research 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.⁴³

(b) The PI 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 PI 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 PI should consult with the applicable IRB to determine whether an addendum to the consent for continued data collection may be used.

7.2.3. Wards.

(a) Research Projects involving children as defined under Federal and New York State law who are wards of the state or any other agency, institution, or entity may participate in a Research Project only if the IRB determines the Research Project is related to the Human Subject's status as wards, and is conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.⁴⁴

(b) If the IRB approves a Research Project involving wards, the PI 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 PI(s) or the guardian organization.⁴⁵

(c) In addition, the PI 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. §§ 46.117 and 46.408.⁴⁶

(d) The FRRC or the RA Office in their respective reviews during the Research Approval Process (Section 3) and Renewal of Research 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 Women, Fetuses and Neonates.

(a) HHC 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.⁴⁷ 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 PI should consult with the IRB with respect to the contents of the Informed Consent. Some considerations the PI 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 PI must demonstrate, generally, the following:⁴⁸

(i) The Research Project relates to the study of incarceration, criminal behavior, prisons 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 possibly 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.⁴⁹

7.2.6. Decisionally Incapacitated Adults and Individuals in OMH or OMRDD facilities.

(a) *Use of Surrogate Permission.* HHC holds the ethical position that the use of surrogate permission with decisionally incapacitated adults 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.⁵⁰ This policy does not apply to the conduct of emergency Research under the FDA regulations 21 C.F.R. § 50.24.

(b) *Enrollment of Decisionally Incapacitated Adults in Research.* The IRB may allow the enrollment of decisionally incapacitated adults, 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 decisionally incapacitated adults. The IRB reviewing a protocol that involves decisionally incapacitated adults 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.⁵¹

(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 PI must include in the Research Protocol the following:

(i) Adequate procedures for making and documenting the determination that a prospective Human Subject is decisionally incapacitated or impaired, 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.
(B. 1. A. Fourth bullet point)

(6) Appropriate procedures for the continuing/periodic capacity assessment of decisionally incapacitated subjects 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 PI must obtain 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) HHC recognizes the health care surrogate pursuant to the New York State Family Health Care Decisions Act⁵² 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 subject and provides

a signed written statement (in a format approved by the IRB) to the PI that they are a close friend of the subject and that they have maintained such regular contact with the 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

(1) offers no prospect of direct benefit to the decisionally incapacitated individual and

(2) involves either a minor increase over minimal risk, or more than a minor increase over minimal risk,

HHC 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 a decisionally incapacitated individual into such Research Project.

(v) For Research that offers the prospect of direct benefit to the decisionally incapacitated individual, HHC 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 decisionally incapacitated Human Subject.

(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 decisionally incapacitated individual into a Research Project, such decisionally incapacitated individual shall not be enrolled in such Research Project.

(vii) If the decisionally incapacitated individual evidences any objection, verbal or otherwise, to being enrolled in the Research Project, such decisionally incapacitated individual shall not be enrolled in such Research Project.

(e) *PI Responsibilities in Obtaining Informed Consent from Legally Authorized Representatives.* When obtaining an Informed Consent from a legally authorized representative (LAR) the PI must do the following:

(i) Provide a notice to the potential participant and LAR that an assessment will be conducted on the potential participant and the consequences (if any) of a determination of incapacity.

(ii) Disclose relevant information to LAR and participant of how the study will be conducted.

(iii) Communicate to the LAR and participant the anticipated risks and benefits to the potential participant of the proposed Research, utilizing a process to facilitate discussion and true understanding of such risks and benefits of participation.

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

(v) 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.

(vi) Communicate to the LAR and the participant if there is no direct benefit to the potential participant from the proposed Research.

(vii) Provide regular updates to the LAR and participant on the status of the participant and the progress of the Research Project.

(viii) PI should analyze whether the LAR 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.

(ix) PI must give the LAR a copy of the “*Guidance for Legally Authorized Representatives Enrolling Decisionally Incapacitated Individuals in Research Studies*”, attached here to as **Exhibit 6** and explain the guidance to the LAR.

(x) Once the LAR has signed the acknowledgement on the “*Guidance for Legally Authorized Representatives Enrolling Decisionally Incapacitated Individuals in Research Studies*”, the signed guidance should be appended to and maintained with the Informed Consent.

(xi) 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 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 decisionally-incapacitated adults who are incompetent persons or mentally disabled persons, the consent of the Commissioner of Health is required, in addition to the consent of the LAR.⁵³

(g) *Release of Clinical Records.* For HHC 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 RA Office and any other applicable committee specially constituted for the approval of Research Projects at the Facility and HHC, provided that the researcher shall in no event disclose information tending to identify a patient or client.⁵⁴

7.2.7. Alcohol and Substance Abuse Patients.⁵⁵

(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 abuse 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 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 of Clinical Records.* For HHC 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 RA Office and any other applicable committee specially constituted for the approval of Research Projects at the Facility and HHC, provided that the researcher shall in no event disclose information tending to identify a patient or client.⁵⁶

7.2.8. Research in Schools.

(a) When a Research Project will be conducted in schools, the PI must, in addition to DHHS 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)⁵⁷ and Protection of Pupil Rights Amendment (PPRA)⁵⁸ are adequately met as described below. FERPA defines the rights of students and parents concerning the reviewing, amending, and disclosing of educational records. Research Projects involving surveys in schools are regulated under PPRA.

(b) The PI, 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;⁵⁹

(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;⁶⁰

(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);⁶¹

(v) compliance with the requirements of the New York City Department of Education Research Proposal Guidelines.⁶²

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 PI must demonstrate that 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.

The economically or educationally disadvantaged,⁶³ 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 PI 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) helps researchers protect the privacy of Human Subjects enrolled in biomedical, behavioral, clinical and other forms of sensitive Research by preventing the forced disclosure of identifying information or identifying characteristics of a Human Subject by the PI through legal demands, such as court orders and subpoenas.⁶⁴ CoCs help achieve the Research objectives of and promote participation in studies by helping assure confidentiality and privacy to participants.⁶⁵ However, a CoC does not protect against voluntary disclosures by the PI, which must be specified in the Informed Consent, and disclosures to DHHS as required for program evaluation or audits, or required disclosures to the FDA. A PI may not rely on the Certificate to withhold data if the participant consents in writing to the disclosure.

CoCs are issued by DHHS's National Institutes of Health and other HHS agencies. A Principal Investigator should consider requesting a CoC for any Research Project that involves personally identifiable, sensitive information and that has received approval from an IRB or IRB approval conditioned on obtaining a CoC. There is no requirement that the Research Project be supported by federal funding in order to receive a CoC.

Identifying characteristics such as: name, address, social security or other identifying number, fingerprints, voiceprints, photographs, genetic information or tissue samples, or any other item or combination of data about a research participant which could reasonably lead, directly or indirectly by reference to other information that identifies the Human Subject.⁶⁶

Sensitive information includes (but is not limited to):

- information relating to sexual attitudes, preferences, or practices;
- information relating to the use of alcohol, drugs, or other addictive products;
- information pertaining to illegal conduct;
- information that, if released, might be damaging to an individual's financial standing, employability, or reputation within the community or might lead to social stigmatization or discrimination;
- information pertaining to an individual's psychological well-being or mental health; and
- genetic information or tissue samples.⁶⁷

Research projects involving these categories of sensitive information are eligible to apply for CoCs; however, the NIH is not required to grant a CoC to every Research Project collecting or generating such information.

A PI is not required to apply for a CoC for Research Projects supported by the Agency of Healthcare Research and Quality,⁶⁸ or covered by the Department of Justice confidentiality statute at 42 U.S.C. § 3789g.⁶⁹

8.2. Procedure:

8.2.1. When to Seek a CoC. Generally, Principal Investigators should consider seeking a CoC whenever sensitive information will be collected or generated during the course of a proposed Research Project in order to promote participation by potential Human Subjects. The Research Council shall develop guidelines for PIs to assist them in determining when to apply for a CoC.

8.2.2. CoC Applications.

(a) Where the PI applies for a CoC, both the PI and Institutional Official must sign the CoC application.

(b) 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.

8.2.3. Changes in Research Protocol. The PI is responsible notifying the NIH 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.

8.2.4. Extension of CoCs. Where a Research Project extends beyond the expiration date of the CoC, the PI 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.

8.2.5. 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.

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

SECTION 9. CONFLICTS OF INTEREST IN RESEARCH

9.1. 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 HHC 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 HHC 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 HHC.

“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 HHC’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 HHC which include, but are not limited to, Research, Research consultation, teaching, professional practice, HHC 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 the U.S. Department of Health and Human Services, and any components of the PHS to which the authority involved may be delegated, including the National Institutes of Health (“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 HHC pursuant to Section 9.3.2(a) of this Section.

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

9.2. **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 HHC responsibilities, and the obligations of HHC in reviewing, monitoring and reporting these interests.

HHC 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, PIs and Research Team members may have additional conflict of interest reporting obligations to the FDA and trial sponsor.⁷⁰

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, PIs and Research Team members who are directly employed by HHC 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 HHC’s Code of Ethics. Further, all Research Team members, whether employed directly or through an affiliation agreement or otherwise, must adhere to the HHC’s Principles of Professional Conduct.

9.3. **Procedures**

9.3.1. Designation of Responsible Parties; Responsibilities.

(a) *Conflicts of Interest in Research Official.* HHC 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 PIs.

(b) *COIR Committee.*

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

(2) COIR Committee shall include (i) HHC’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 HHC, 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 HHC 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 9.3.4(b)(i)(4).

(iv) The RA Office 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 9.3.2(a)(i).

(v) Covered Individuals shall be responsible for:

(1) disclose their Significant Financial Interests, or those of their spouses or dependent children, as required under Section 9.3.2.

(2) complying with the SFI review process as set forth in Section 9.3.4

(3) completing training as required under Section 9.3.7.

9.3.2. Disclosure of Significant Financial Interests.

(a) *Initial and Annual Disclosures.*

(i) Covered Individuals must disclose certain financial interests and non-HHC 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 7**). The SFI Disclosure Form must be completed and submitted by the Covered Individual to the RA Office with each application or proposal submitted for funding, and annually during the period of any award or contract. The RA Office 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.

9.3.3. Subrecipient Requirements. Where Research is carried out through a Subrecipient, HHC and the Subrecipient must comply with the following:

(a) *Written Agreement.* HHC 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 HHC sufficient to enable HHC to provide timely FCOI Reports, as necessary, to governmental agencies as required by federal and state law and regulations.

(c) *Application of HHC 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 HHC sufficient to enable HHC to comply timely with its review, management, and reporting obligations as required by federal and state law and regulations and this Section.

9.3.4. 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 RA Office. The RA Office 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 HHC 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 HHC, 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 HHC is considering a possible conflict of interest with the understanding that HHC will not approve the Research Project unless the conflict can be managed or eliminated. HHC 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 9.3.4(d).

(ii) **Review of SFIs not Timely Disclosed.** Whenever HHC 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 PART II 9.3.4(d); and

(3) conduct a retrospective review, as described below in Section 9.3.4(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 HHC to constitute a Financial Conflict of Interest;

b. failure by HHC 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) HHC 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, HHC 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, HHC will notify the PHS Awarding Component promptly and submit a Mitigation Report to the PHS Awarding Component, as described in Section 9.3.5(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 PI, 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 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.

9.3.5. HHC Reporting Requirements to NIH.

(a) *FCOI Reports.*

(i) *Initial FCOI Report.* Prior to HHC's expenditure of any funds under a PHS-funded Research Project, HHC shall provide to the PHS Awarding Component an FCOI Report regarding any FCOI and ensure that HHC has implemented a management plan in accordance with Section 9.3.4(d). In cases in which HHC 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 HHC with regard to an ongoing PHS-funded Research Project, HHC 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 an Covered Individual who is new to the Research Project or upon transfer of a Research Project from another institution), HHC shall provide within sixty (60) days to the PHS Awarding Component a FCOI Report ensuring that HHC has implemented a management plan in accordance with Section 9.3.4(d).

(iv) *Report Contents.* All FCOI reports required under this Section 9.3.5(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 HHC'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 9.3.4(c)(ii)) HHC must provide to the Research Project's PHS Awarding Component a Mitigation Report if it is determined in its retrospective review discussed in Section 9.3.4(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, HHC will promptly notify the PHS Awarding Component of the corrective action taken or to be taken.

(d) *Submission Procedure.* HHC 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.

9.3.6. 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 HHC'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 HHC'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 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.

9.3.7. Training.

(a) *Initial Training.* HHC 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. HHC 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) HHC 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 HHC; or

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

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

9.3.8. 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 HHC'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 HHC as required by this Section, HHC 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.

9.3.9. Public Accessibility.

(a) *Public Access to this FCOI Policy.* HHC 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 HHC's expenditure of any funds under a PHS-funded Research Project, HHC 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

HHC requires the dissemination of Research knowledge in the public interest. If this Research knowledge is acquired in work involving Human Subjects at HHC and/or using HHC resources, and is disseminated through publications, abstracts, presentations, or posters, HHC is required to be acknowledged per the guidelines listed below. HHC and its employees have a responsibility to ensure that HHC 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 RA Office 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

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

10.2.1. Notification Process.

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

(b) HHC will strictly adhere to embargoes put in place by the journals and will notify the PI before issuing any press release or publication regarding the respective Research Project. Once published, HHC 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 HHC Research Support/Resources/Employment.

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

(i) If HHC provided direct Research funding, the publications or presentations, “This material is based upon work supported (or supported in part) by the New York City Health and Hospitals Corporation”.

(ii) If HHC provided no direct Research funding, but the Research involved the use of other HHC resources (e.g., HHC Facilities or patients) and is not a multi-site trial, the publications, or presentations must contain an acknowledgement of HHC or the Facility as appropriate.

(b) *Acknowledgement of HHC Affiliations.* Authors of clinical and Research publications, abstracts, and presentations must acknowledge their affiliation using the following format, if permitted by the journal: “HHC Department, HHC 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 HHC generally, as permitted by the journal.

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

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

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

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

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

SECTION 11. INVENTIONS

11.1. 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 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 HHC 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 HHC 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.

11.2. Policy

It is the intent of HHC, in administering intellectual property rights for the public benefit, and to encourage and assist members of the faculty, staff, and others associated with HHC 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.

HHC 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 HHC, 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 HHC employment or other duties at or for HHC; (2) in connection with research or clinical activities at or under the auspices of HHC; (3) with substantial use of HHC 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 HHC. Any and all exceptions to this policy shall be determined and approved by the President of HHC in consultation with the Intellectual Property Committee (IPC) and Office of Legal Affairs.

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

11.3. **Procedure**

11.3.1. **Disclosure and Filing.**

(a) *Disclosure.* All HHC employees and staff shall promptly disclose all Inventions to the RA Office using the Inventions Disclosure Form, attached as **Exhibit 8**. Upon receipt of the completed Inventions Disclosure Form, the RA Office will:

(i) In his or her 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 HHC has entered, HHC 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. HHC shall use reasonable efforts to successfully commercialize such Invention.

11.3.2. Confidential Information. As a condition of employment/appointment with HHC, employees/staff shall hold in strictest confidence any confidential information, which includes any of HHC's proprietary 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 HHC 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 HHC. 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 (HHC) 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 RA Office, the IPC will review the disclosure within 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 HHC's interests, 2) recommending to HHC 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 HHC'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 HHC'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 HHC, 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 HHC's intention to file a patent application or otherwise to retain title to the Invention after disclosure to HHC of an Invention.

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

(3) Receive from HHC title to any Invention subject to this Policy in the event HHC 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 HHC-owned Invention, report promptly to the HHC IPC through the Invention Disclosure Form a summary of the concepts, relevant data, observations and general claims with respect to any invention, discovery or development, as well as the name(s) of any collaborator(s);

(ii) Assign right, title, and interest to the discovery or invention to HHC;

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

(iv) Cooperate to the extent necessary as determined by HHC 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 HHC 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 discovery or invention.

(c) *HHC Obligations.* HHC is obligated to:

(i) Assign to the Inventor title to any Invention subject to this Section for which HHC 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 HHC, and exclude others from doing so;

(iii) Make PIs 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 HHC and Affiliate resources;

(v) After an Invention is disclosed, act in a timely fashion to determine whether HHC 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 a discovery or invention, of HHC's decision to file a patent application or otherwise retain title to the discovery, invention or development;

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

(viii) Distribute licensing fees or royalties received by HHC for any discovery, Invention or development according to the distribution of proceeds described in Section 11.3.6.

11.3.5. Licensing. HHC 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. HHC 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, HHC shall allocate the first monies to the payment of any and all fees and costs, including legal counsel fees incurred by HHC in obtaining any patent protection.

(b) After this deduction by HHC, 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) HHC 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. HHC CONTINUING APPROVAL

12.1. Policy

In order to fulfill the assurances given to the federal government by HHC under its FWA during the course of a Research Project for which initial approval has been obtained under Section 3, Facilities must regularly review the progress and safety of the Research Project and request continuing approval of the Research Project in accordance with the procedure below. Research Projects that are exempt from IRB review pursuant to law, as determined in consultation with the applicable IRB,⁷¹ are not subject to this renewal process.

12.2. Procedures

12.2.1. IRB Progress Report and Continuation Letter. The PI will submit a copy of the IRB annual report and the IRB continuation letter into STAR. These documents must be submitted to STAR prior to the IRB date of expiration listed in STAR.

12.2.2. Automatic Continuing Approval. If there have been no Major Protocol Violations (as described in Section 22 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 31.1) to be sufficient to cover the next year's expenses, then the Research Project will be automatically renewed at the Facility level for a term of no greater than one (1) year based on the IRB expiration date.

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. Notification of Continued Funding. In all cases, the PI will provide the Facility with a copy of the IRB approval notice and written notice of continued external funding if the Facility does not already have it, which may be copies of written notification from the Grantor or Sponsor, within thirty (30) days of PI receiving such approval or notice.

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

12.2.6. Notice to RA Office. Once a Facility has renewed its approval to continue a Research Project, the RA Office shall be notified via STAR.

SECTION 13. SUSPENSION & TERMINATION OF RESEARCH PROJECT

13.1. **Policy**

In order to protect HHC's and its researchers' financial, contractual, and legal interests, HHC 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 HHC Approval process discussed above in Section 3 and Section 12.

Additionally, all Research Projects that have received HHC approval or continuing approval through STAR are subject to suspension if their IRB documents (progress reports and continuation letters) are not submitted to STAR prior to the IRB date of expiration listed in STAR or if deemed necessary by Facility, Corporate Administrators, Sponsors or IRBs.

Subject to law and the terms of the governing Research agreement, if applicable, HHC 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 can suspend or terminate a Research Project if deemed necessary.

(a) HHC 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 PI, the FRC will suspend the project in STAR. The PI 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, HHC may suspend enrollment of all Human Subject or terminate a Research Project if HHC, in consultation with the IRB and PI, has determined that there are Human Subject safety concerns, or based on financial or administrative reasons.

13.2.2. *Failure to Update IRB Documents.* PIs must keep all IRB documents current in STAR. Failure to do so will result in an automatic suspension based on the IRB expiration date entered in STAR. A PI will have up to 10 business days after the IRB expiration date to upload the appropriate IRB documents. After 10 business days, the project will be suspended and the PI will be required to renew and start a new application.

13.2.3. *Continuity of Care.* Upon termination or suspension of a Research Project under this section, the PI shall provide a plan for the continuity of medical care for current Human Subjects withdrawn from such Research Project in accordance with OHRP guidance,⁷² PI'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 at the completion of the project, or earlier if terminated or suspended prior to the Research Project's completion.

14.2. **Procedure.**

14.2.1. PIs must request closure of each Research Project in STAR to the FRC. A closeout or termination letter from the IRB should be submitted as part of this closure. The FRC is responsible for reviewing the PI's request and ensuring that the study is closed within STAR.

14.2.2. FRCs retain the right to close or terminate a study in STAR without the request of the PI, if deemed necessary by Facility, corporate administrators, Sponsors or IRBs.

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

15.1. **Policy**

HHC 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, HHC will conduct quality assurance activities and ensure that any of its contractors conduct their responsibilities with respect to Research in accordance with HHC's quality assurance requirements and obligations, to the extent applicable. Research Projects are eligible for monitoring and full audits by HHC after the first Human Subject is enrolled.

In instances where HHC has delegated the review of Research Protocols under its FWA to an outside IRB, HHC 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 RA Office can request the monitoring reports from Sponsors or the Principal Investigator, if applicable. If the RA Office has made a

determination to conduct an independent investigation, the RA Office, 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 HHC. 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 PI 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 HHC;
- (b) Informed Consent, assent, parental permission document(s), if applicable, and Research Authorization Form as approved by HHC 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 HHC RA Office 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 HHC Operating Procedure 40-59: Time and Effort Reporting and Operating Procedure;
- (h) All correspondence between investigators, RA Office, Grantor/Sponsor and reviewing IRB(s); and
- (i) Any other documentation as determined by the IRB and HHC.

15.2.2. Audits.

(a) *Frequency and Scope.* The RA Office, 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 PI 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 RA Office. The RA office will work with the PI 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 HHC Operating Procedure 30-1.

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 HHC Operating Procedure 50-1 (Corporate Compliance Program) or any other applicable HHC policy or procedure.

(c) *Independent Audits and Monitoring.* HHC 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 HHC 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 HHC Operating Procedure 50-1 (Corporate Compliance Program).

PART IV

INVESTIGATIONAL DRUGS, DEVICES, AND BIOLOGICAL MATERIALS

SECTION 16. STORAGE, HANDLING & DISPENSING INVESTIGATIONAL DRUGS & BIOLOGICS

16.1. Definitions

For purposes of this Section 16, 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.⁷³

“**Investigational Brochure**” or “**IB**” refers to a comprehensive document summarizing all known information about an investigational agent.⁷⁴ 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.

“**Investigational Drug**” means a new drug that has not yet been approved by the FDA or approved drugs that have not yet been approved for a new use and are in the process of being tested for safety and effectiveness.

“**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.⁷⁵

16.2. Policy

All Investigational Drugs, agents, or Biologics in use at an HHC Facility must be stored, handled, and dispensed in accordance with FDA, Federal and New York State Boards of Pharmacy regulations and guidance,⁷⁶ and HHC policies and procedures. Controlled substances in use at HHC Facilities are also subject to particular licensing requirements under federal and New York state laws.

16.3. Procedures

16.3.1. 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.⁷⁷

(b) *Facility Pharmacy/Pharmacist.*⁷⁸ 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,⁷⁹ 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.⁸⁰

- (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 9**) described in Section 16.3.3.⁸¹
- (vii) Retaining the Research Protocol documents and Investigational Drug Accountability Log maintained by the Facility Pharmacy according to HHC policy and procedures with respect to Research records, FDA regulations or Sponsor/Grantor requirements, whichever time period is longest.⁸²
- (viii) Obtaining approval from the Sponsor/Grantor prior to destroying records.
- (ix) Obtaining a signed Informed Consent form prior to dispensing an Investigational Drug.
- (x) Making available for inspection by the Study Monitor a patient specific source chart.

16.3.2. Investigational Drug and Supply Management. All Investigational Drug and supply management must remain under the direction of the Facility Pharmacy.⁸³

16.3.3. 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 PIs 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 10** can be used in negotiations. An LOU can exist between a Facility and an HHC affiliate, provided that investigators at the Facility and HHC affiliate are both participating in the Research Project utilizing the Investigational Drug.⁸⁴

(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 9**).

16.3.4. 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,⁸⁵ 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 9**) or an accountability record, authorized by HHC 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 9**, must be compliant with the FDA's regulations governing electronic records and electronic signatures.⁸⁶

(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 HHC 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 HHC 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 PI 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.

16.3.5. 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, HHC 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.”⁸⁷

(g) If compounding or admixing of the Investigational Drug is required by the Research Protocol, applicable United States Pharmacopoeial Standards⁸⁸ and Good Clinical Practices must be followed.

(h) If a Sponsor or Grantor has additional dispensing requirements, these must be followed.

16.3.6. 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.⁸⁹

(b) Investigational Drugs and supplies returned by Human Subjects may not be re-dispensed.⁹⁰

(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 17. MATERIAL TRANSFER AGREEMENTS

17.1. Policy

HHC 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 HHC and researchers from liability relating to the transfer and subsequent use and handling of the material, as well as to ensure HHC's and researchers' publication and intellectual property rights in the material, Principal Investigators must work with the RA Office 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 11** for an example of HHC's MTA template.

17.2. Procedure

17.2.1. Sending Material:

(a) To send materials outside of HHC, the Principal Investigator must email the FRC, who will then notify the RA Office, 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 RA Office will forward the appropriate documents to OLA for review and approval. Upon OLA approval, the RA Office will forward the documents to the receiving party and notify the PI when signatures have been obtained, thus allowing the PI to send the materials.

17.2.2. Receiving Material.

When seeking to acquire material from outside of HHC, 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 RA Office. The RA Office will consult with and obtain final OLA approval of the documents to protect the PI's publication and other intellectual property rights, and to comply with HHC policies. The RA Office will keep the PI informed throughout the negotiation process, and will provide the PI with a fully executed copy of the MTA.

SECTION 18. USE OF TRANSFERRED BIOLOGICAL MATERIALS

18.1. Definitions.

For purposes of this Section 18, 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.

18.2. Policy

All Research conducted outside of a Research Protocol using Biological Materials shall be conducted in accordance with the applicable MTA (see Section 17, Material Transfer Agreements), Informed Consent and all applicable State and Federal laws regarding such Research. The PI 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.

18.3. 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 17 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 HHC's Office of Legal Affairs.

SECTION 19. GUIDELINES FOR USE AND DISCLOSURE OF GENETIC INFORMATION

19.1. Definitions

For purposes of this Section 19, 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 19.3.7(a).

19.2. 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, HHC requires that a consent conforming to the requirements of 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 consent may be part of the Informed Consent. A model Informed Consent for Research Involving Genetic Testing is attached at **Exhibit 12**. To the extent a Research Project is reviewed by the IRB of an Affiliate, HHC will collaborate with that IRB to ensure the consent and corresponding genetic testing conforms to HHC’s requirements.

Moreover, genetic information must also be kept confidential and be disclosed only as described in Sections 19.3.6 and 19.3.7. 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, PIs must consult and comply with the Clinical Laboratory Standards of Practice for genetic testing set forth by the NYSDOH Wadsworth Center⁹¹ and the NIH Genomic Data Sharing Policy.⁹²

19.3. Procedures

19.3.1. Conducting Genetic Testing as Part of Research.

(a) *Informed Consent.* Unless the Biological Sample is anonymous pursuant to Section 19.3.3, if conducting a Genetic Test on a Biological Sample is part of the Research Protocol then such Genetic Test may not be conducted unless a separate consent, the form of which is found in **Exhibit 12**, is obtained from the Human Subject specifically 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.

(b) *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.⁹³

(ii) *Extension Past the Sixty Days.* With the approval of the IRB and the written consent of the Human Subject, described in Section 19.3.2, the biological sample may be kept for longer than 60 days and utilized for Research purposes.⁹⁴

19.3.2. 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.⁹⁵

(b) The requirements of Section 19.3.2(a)(iv), (v) and (vi) may be modified by the IRB in case the Research Protocol does not permit such degree of specificity.⁹⁶

19.3.3. Using Anonymous Biological Samples.

Genetic Tests may be performed on Biological Samples for which there is no identifiable individual from whom to obtain consent, provided that the IRB determines that the Research Protocol submitted by the PI assures the anonymity of the sources of the samples.⁹⁷

19.3.4. 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 on a form the template for which is found in **Exhibit 12**;

(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.⁹⁸

(b) Content of written consent to use stored Biological Samples must contain at least the following:

(i) a statement that the sample will be used for future genetic tests;

(ii) the time period during which the tissue will be stored, or if no time limit is specified, a statement that the tissue will be stored for as long as deemed useful for Research purposes;

(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 tissue, 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.

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) *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.⁹⁹

19.3.5. Additional Language Regarding Protections under the Genetic Information Nondiscrimination Act.¹⁰⁰

HHC 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:¹⁰¹

“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.”

19.3.6. 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. PIs 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 HHC HIPAA Clinical Investigation and Research Policy and Guidelines, Operating Procedure 240-23, Appendix E.

19.3.7. 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 19.3.6(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 HHC 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.¹⁰²

(See also HHC HIPAA Clinical Investigation and Research Policy and Guidelines, Operating Procedure 240-23, and OHRP's *Guidance on the Genetic Information Nondiscrimination Act: Implications for PIs and Institutional Review Boards*).¹⁰³

19.3.8. Decedent Data and Genetic Testing.

(a) Where a PI seeks to perform genetic testing on decedent specimens, HHC requires that the PI seek a special waiver regarding the use of decedent information. HHC 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.¹⁰⁴

19.3.9. 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.¹⁰⁵ Therefore, there are certain steps that must be taken prior to storing and/or using genetic samples for research purposes. (See also HHC 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 PI must obtain a consent that complies with both New York consent requirements (which are listed in Section 19.3.4(b)) and a HIPAA Research Authorization Form for storage purposes. (See also HHC 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 PI 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 19.3.4(b)). (See also HHC 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 HHC shall promptly destroy the sample or portions thereof that have not already been used for research purposes.¹⁰⁶

19.3.10. 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.¹⁰⁷ Consent in the form of the template in **Exhibit 12** must be obtained before Genetic Testing may be performed on the stored sample.

SECTION 20. GUIDELINES FOR USE OF ANATOMICAL GIFTS

20.1. Policy

Under New York State's Uniform Anatomical Gift Law,¹⁰⁸ 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.¹⁰⁹

20.2. Procedures

When HHC, a Facility, PI 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 HHC 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 21. RESEARCH MISCONDUCT

21.1. Definitions

For purposes of this Section 21, 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 HHC Anonymous Reporting Line (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 21.2.1.

“**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.

21.2. Policy

21.2.1. General. HHC 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.

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.

21.2.2. Applicability.

This Section 21 applies to allegations of Research Misconduct involving:

(a) all individuals at HHC engaged in Research. This policy applies to any person paid by, under the control of, or affiliated with HHC, such as principal investigators, trainees, technicians and other staff members, students, fellows, guest researchers, or collaborators at HHC; 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.

21.3. **Procedure**

21.3.1. **Roles and Responsibilities.**

(a) *HHC Chief Medical Officer.* The HHC Chief Medical Officer shall be responsible for handling all Allegations of Research Misconduct. The HHC 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 HHC 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 HHC Operating Procedure 30-1.

(b) *The Coordinator.* The HHC Chief Medical Officer shall designate an individual who serves in the RA Office to act as a coordinator (“Coordinator”) to assist in carrying out this Section 21. The Coordinator shall act as a neutral facilitator, but shall consult with the HHC Office of Legal Affairs to ensure that the requirements of law and HHC 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 HHC Chief Medical Officer in administering the process of any inquiry or subsequent investigation, shall:

(i) Advise members of the HHC community in response to requests for information or informal consultation concerning Research Misconduct;

(ii) Keep the HHC Chief Medical Officer informed of any Allegations filed and the progress of any inquiry or investigation undertaken;

(iii) Notify the HHC Office of Inspector General of any inquiries from federal, state and local law enforcement agencies with respect to alleged Research Misconduct in accordance with HHC Operating Procedure 30-1;

(iv) Work with and advise the various HHC officials and committees involved in the inquiry and/or any subsequent investigation or disciplinary action. The Coordinator shall offer advice regarding HHC 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 HHC 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 HHC 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) HHC 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 HHC 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 HHC 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 HHC's control, custody, or possession and access to all persons within its authority necessary to develop a complete record of relevant evidence.

21.3.2. 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 HHC Anonymous Reporting Line (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.

21.3.3. 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 21.2.1. 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 HHC Office of Legal Affairs serves as an advisor to HHC 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 HHC 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 HHC'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 HHC 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 21.2.1 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 21 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.

21.3.4. 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.*

(1) In making appointments to the COI, the CMO shall appoint at his or her discretion individuals with the following qualifications:

a. Individuals with appropriate scientific and/or academic expertise to evaluate the evidence and issues related to the Allegation;

b. Individuals free from bias and any real or apparent personal, professional or financial conflicts of interest with the Complainant or Respondent;

c. At least one individual who has acted as the Principal Investigator for a Research Project in the last five years. This individual(s) cannot be affiliated with the Facility at which the Allegation has occurred;

(2) 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) HHC 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, HHC 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:¹¹⁰

(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 HHC, 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 HHC, 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 HHC, 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.

21.3.5. Investigation. When a COI determines that the Allegation has substance through the inquiry process described in Section 21.3.4, an investigation will be initiated. Such investigation and any disciplinary sanctions, if necessary, shall comply with HHC policy and practice, as well as with this Section 21 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 years who is not affiliated with the Facility at which the Allegation has occurred; and

c. Any other persons inside or outside HHC, 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.

21.3.6. Sanctions. Appropriate sanctions shall be imposed by HHC when a final investigation report finds that Research Misconduct has occurred. Sanctions shall be commensurate with the severity of the Research Misconduct.

21.3.7. Notice to ORI of Findings and Actions. HHC 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 HHC found Research Misconduct, and if so, who committed the misconduct;
- (c) A statement as to whether HHC accepts the investigation's findings; and
- (d) A description of any pending or completed administrative actions against the Respondent.

21.3.8. Correction of Erroneous Research. If Research Misconduct has been found under Section 21.3.5 and erroneous Research Project Data has been published, the Respondent will work with HHC 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, HHC, working with the researchers involved, will seek to correct the published record.

21.3.9. 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 HHC Office of Inspector General in accordance with HHC Operating Procedure 30-1.

21.3.10. Time Limitations. The requirements set forth in this Section 21 apply only to Research Misconduct occurring within six years of the date HHC 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 HHC, 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 HHC received the Allegation of Research Misconduct before the effective date of these Policies and Procedures.

21.3.11. 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 HHC does require that the Complainant be identified as the ‘complainant’ but HHC 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.

HHC 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 HHC employees against good faith Complainants, witnesses or committee members shall result in disciplinary action under appropriate HHC rules, policies or procedures.

21.3.12. Confidentiality. HHC 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.

21.3.13. Restoration of the Respondent’s Reputation. Following a final finding that Research Misconduct did not occur, HHC 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 HHC Chief Medical Officer.

SECTION 22. PROTOCOL VIOLATIONS AND DEVIATIONS

22.1. Definitions

For purposes of this Section 22, 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 PI without prior IRB approval.¹¹¹ 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.¹¹²

22.2. Policy

HHC requires all Major Protocol Deviations and Major Protocol Violations to be reported as set forth below.

22.3. Procedures

22.3.1. Protocol Violations. All Major Protocol Violations that occur in an HHC Facility must be reported by the PI to the RA Office, the Medical Director and applicable IRB in accordance with the timeframe and process set forth in the IRB’s policies and procedures.

22.3.2. 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 HHC.

22.3.3. 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 HHC approval.¹¹³ Any such changes should be reported to the IRB as soon as possible after they occur.

22.3.4. Other Reporting Requirements. Sponsor or Grantor reporting requirements for such deviations may differ from Affiliate reporting requirements. PIs should be aware that agreements entered into with the Sponsor or Grantor with respect to a Research Project may require the PI to notify the Sponsor or Grantor of all Protocol Violations, including unplanned deviations or departures from IRB-approved protocol procedures. It is the PI's responsibility to comply with the reporting requirements outlined in the signed contract or protocol with the Grantor or Sponsor. Before a PI acknowledges and agrees to the terms of a Research agreement, the PI is strongly advised to read and understand the contract terms, working with the RA Office and/or HHC's Office of Legal Affairs which will promptly advise PIs, as needed, prior to signing. Final approval will be obtained from the RA Office and OLA.

SECTION 23. REPORTING OF UNANTICIPATED PROBLEMS

23.1. Definitions

For purposes of this Section 23 , 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 subjects.¹¹⁴

“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 may be 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 23.2.2.

“Unrelated” means unassociated or without a timely relationship; evidence exists that an outcome is definitely related to a cause other than the event in question.

23.2. Policy

23.2.1. HHC 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.¹¹⁵ Accordingly, HHC requires PIs to promptly report all Unanticipated Problems and all Serious Adverse Events that occur at an HHC Facility as set forth below.

23.2.2. Unanticipated Problem Involving Risks to Human Subjects or Others, in general, include any incident, experience, or outcome occurring at an HHC Facility 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.

23.3. Procedures

23.3.1. 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. PIs should adhere to the policy of the IRB overseeing a Research Project with regard to timely reporting required events.

23.3.2. 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 RA Office, 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 22 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.

23.3.3. Events Which are Not Immediately Reportable. Potential risks and adverse events occurring at an HHC 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).

23.3.4. Parallel Reporting Requirements.

(a) *Institutional Reporting.*

(i) The RA Office, in accordance with the terms of HHC’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 30 days.

(ii) The Facility Research Administration Offices will ensure that any other department or individual within the Facility and HHC, 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 HHC’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 HHC’s Office of Compliance as necessary to mitigate and manage any such breach.

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 24. REPORTING NONCOMPLIANCE

24.1. **Policy**

Federal regulations require that HHC has written procedures for ensuring prompt management of any instances of serious or continuing non-compliance with OHRP policy.¹¹⁶ 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 HHC in connection with Research, has the duty and responsibility to report such noncompliance to the FRRC Chair, IRB and appropriate institutional officials.¹¹⁷ HHC 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.

24.2. **Procedure**

24.2.1. *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 RA Office. The RA Office 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-HELPHHC).

(c) Instances of conduct involving fraud, abuse, and waste with respect to billing, coding, and time and effort reporting, must be reported to the RA Office, 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-HELPHHC).

(d) Instances of conduct involving non-compliance that might be criminal in nature must be reported to the RA Office and the HHC Office of Inspector General, and should also be simultaneously reported to the IRB. The Office of Inspector General Hotline is 212-676-0942.

24.2.2. *Verbal Reports.* If a verbal report is received, the individual who made such report may be required to subsequently submit a written report.

24.2.3. *Investigation.* All allegations will be promptly investigated by the RA Office, 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.

24.2.4. *Confidentiality.* All matters will be reviewed confidentially to the extent possible and as warranted by the situation.

SECTION 25. NON-RETALIATION AND PROTECTION OF WHISTLEBLOWERS

25.1. **Policy.**

No member of the Research Team or other individual employed by, on staff at, or otherwise affiliated with HHC shall be discriminated against or be subject to reprisal for reporting in good faith 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 in good faith may itself be considered serious non-compliance with HHC policies and procedures, and will result in disciplinary in accordance with HHC policies and procedures.

25.2. **Procedure.**

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

PART VI

RESEARCH RECORDS, REIMBURSEMENT, COSTS & REPORTING

SECTION 26. RESEARCH RECORDS

26.1. Definitions

For purposes of this Section 26, 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.

26.2. Policy

In order to ensure that HHC 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 HHC, HHC is responsible for maintaining and providing access to Research Records in accordance with its contracts with Sponsors and Grantors and applicable law.

26.3. Procedures

26.3.1. All Research Records shall contain all information required by law.¹¹⁸

26.3.2. 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.

26.3.3. Where a contract between HHC and a Sponsor or Grantor requires HHC to retain Research Records for a period that is longer than that required by law, HHC will adhere to that contractual retention period.

26.3.4. PIs or their designee shall include all Research Project Data in the Research Record along with source documents.

26.3.5. All Research Records must be maintained and disposed of in accordance with applicable provisions of HHC Operating Procedure 120-19, HHC record management policies, and applicable law.

26.3.6. In addition to the foregoing, the Facility must retain Research Records for ¹¹⁹seven (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, ¹²⁰ and must make them available to HHC, upon request, in a manner that is consistent with the confidentiality and rights of the Human Subjects. (Please see HHC HIPAA Clinical Investigation and Research Policy and Guidelines, at Sections 8.0 through 8.2 and 9.0, and HHC 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.)

26.3.7. Research Records used in any regulatory or legal matter must be retained in accordance with HHC Operating Procedure No. 120-19. However, prior to disposing of Research Records, OLA 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.

26.3.8. Research Records at HHC must be accessible for inspection and copying by authorized representatives of DHHS at reasonable times and in a reasonable manner.¹²¹

26.3.9. 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.

26.3.10. 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 Rule¹²² 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 abuse, are to be kept in the Human Subject's research folder and become a permanent part thereof.

26.3.11. Any contract between HHC 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.¹²³

SECTION 27. HUMAN SUBJECT AS INPATIENT OR OUTPATIENT

27.1. **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 HHC 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 HHC.

27.2. **Procedure**

The Research Project must be identified at the time of the encounter and related reimbursement methodology must be identified and approved by HHC prior to study implementation.

SECTION 28. RESEARCH RELATED INJURIES: TREATMENT AND REIMBURSEMENT

28.1. **Definitions**

For purposes of this Section 28, 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.

28.2. **Policy**

28.2.1. **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.¹²⁴

This Section defines what treatment HHC will provide to Human Subjects as a result of a Research Related Injury, and defines HHC’s requirements for Sponsors of Research regarding Research Related Injuries.

28.2.2. 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 HHC 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.

28.2.3. Reimbursement for Research Related Injuries.

(a) *For Research Projects Funded by a Sponsor.* The RA Office will review the applicable Research agreement to determine HHC's obligations under this Section. HHC'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.

28.2.4. Limitation of Obligation.

(a) *HHC Obligations.* The obligation of HHC 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 HHC, HHC'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.

28.3. **Procedures.**

28.3.1. Initial Notification and Preliminary Review. HHC'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 PI within a reasonable time after discovery.

(b) The PI 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 23.2.2. In making this determination, the PI should review the Research Protocol, any consent forms signed by the Human Subject, investigator brochure or drug labeling and pertinent medical literature. The PI shall also consult with the IRB as appropriate.

(i) Upon determining that a Human Subject may have suffered a Research Related Injury, the PI must report the claimed Research Related Injury to the Facility's medical director, copying the RA Office, the IRB and the PI's respective FRRC as promptly as possible. Only injuries that the PI 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.

28.3.2. Determination.

(a) The PI will promptly notify the IRB, RA Office and FRRC Chair of all Research Related Injuries. The PI 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 23.2.2. The FRRC will advise the applicable Facility's finance department to flag charges while internal assessments are underway.

(b) The PI together with the IRB will be responsible for making the final determination of whether a Research Related Injury covered by this Section 28 has occurred and resulted directly from the Human Subject's participation in the Research Project.

(c) If the PI 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 29. RESEARCH COSTS

29.1. Definitions

For purposes of this Section 29, the following definitions shall apply.

“Research Project Costs” means the amount due to HHC from an Affiliate when such Affiliate is the Grantee with respect to a specific Research Project and the Research is conducted at an HHC Facility, such amount being calculated under an agreement between HHC and the Affiliate that includes terms for reimbursement of such costs.

29.2. Policy

HHC will work with researchers and Affiliates to encourage research throughout the HHC system. Where research for which an Affiliate is the Grantee is conducted at an HHC Facility, however, HHC 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 HHC (through the approval process outlined in Section 3 and Section 12 of these Policies and Procedures) to be conducted at a Facility by a PI or any person unless HHC and the Facility have reviewed and approved all costs that may be incurred by the accomplishment of such Research, and the Affiliate and HHC have agreed in writing as to how such costs will be reimbursed to HHC.

29.3. Procedures

29.3.1. 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 PI 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 HHC as part of the Research approval process described in Section 3 of these Policies and Procedures. The Facility will obtain all salary and related personnel services information from the Affiliate.

29.3.2. Items To Be Included In Proposed Budget.

The procedure for preparing a proposed budget should be considered with any affiliation agreement and/or research agreement in place between an Affiliate and HHC.

(a) If a research agreement exists between an Affiliate and HHC, 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.

(b) If a research agreement does not exist between the Affiliate and HHC, 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 HHC 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 Legal Affairs. If an Affiliate is a subcontractor to HHC 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.

(c) *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 HHC as subcontractor.

(d) *HHC Direct Costs.* It is the expectation of HHC that HHC employees, HHC agents, or HHC subcontractors, as designated by HHC, 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 HHC employees, agents, or subcontractors will be utilized to participate in such studies.

29.3.3. HHC 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 HHC 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.

29.3.4. Affiliate Costs. Where HHC is the Grantee and where an Affiliate incurs costs due to Research conducted at a Facility, HHC will reimburse that Affiliate for such costs in accordance with any applicable provisions of an agreement with a Sponsor or Grantor and HHC's policies, procedures and applicable law.

29.3.5. 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 HHC Operating Procedure 100-5: Procurement Methods, Required Approvals and Reporting.

29.3.6. Travel Related to Research Project.

(a) The requirements of HHC 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, HHC Operating Procedure 10-10: Official Travel and Miscellaneous Business Expense shall apply.

SECTION 30. RESEARCH TIME AND EFFORT REPORTING

(Please see HHC Time and Effort Policy and Procedure Number 40-59).

SECTION 31. BILLING COMPLIANCE

31.1. Definitions

For purposes of this Section 31, 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 HHC 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 31.3.2(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 31.3.2 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 HHC and/or a Facility who is responsible for any aspect of billing for services or items provided by HHC during the course of research on behalf of HHC 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 HHC 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.¹²⁵

“**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.

31.2. Policy

31.2.1. General. HHC 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 HHC,
- (c) Represented consistently across all award-related documents, including the Research Protocol, Grant, Contract, budget and Informed Consent, and
- (d) Consistent with HHC procedures that establish safeguards to prevent billing mistakes.

31.2.2. Importance of Proper Billing. Billing for clinical research services provided to patients enrolled in research studies 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 HHC 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.

31.2.3. Possible denial of claims and direct liability of PI. 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 HHC. Moreover, HHC could be held liable for such costs and investigations of HHC and the trial’s principal investigator may also be open to more scrutiny by CMS.¹²⁶

31.2.4. Laws, Regulations and Guidance that Affect Billing Compliance.

(a) *45 C.F.R. Part 74*. 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 74, and/or by the terms of the particular Grant.

(ii) The cost must be allocable (i.e., the project that paid the expense must benefit from it).

(iii) The expense must be reasonable (i.e., the cost reflects what a “prudent person” might pay).

(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 2013.* For federally funded clinical trials, HHC is subject to the regulations located in the NIH Grants Policy Statement listed under the heading Routine Patient Care Costs.¹²⁷ Research patients may receive Routine Services as inpatients, or Ancillary Services as either inpatient or outpatient subjects/volunteers. HHC 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.¹²⁸ 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. HHC’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.¹²⁹

(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 Regulations.* Other federal regulations, such as the Anti-Kickback Statute, Stark Laws, Deficit Reduction Act of 2005 and the Federal False Claims Act also govern the billing and management of clinical trials and federal grants and contracts.

31.3. **Procedure**

31.3.1. **Roles and Responsibilities.**

(a) *HHC Facilities.*

(i) Will ensure that a uniform research code will be used in its billing system throughout HHC.

(ii) 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, PI 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 PI and study staff to review and approve rates/fees associated with hospital ancillary services.

(ii) Assist the PI 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 HHC.

(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 studies 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 HHC.

(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 (ORA).*

(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 PI 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.

31.3.2. 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. For clarity, if a Sponsor offers to pay for all visits, treatment and services as part of the draft contract, no Coverage Analysis is needed; however, it is expected that an analysis of coverage of costs for these services was performed by the PI in collaboration with the FFA. 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 no Coverage Analysis is completed because the Sponsor has offered to pay for all visits, treatments and services, the budget received from such Sponsor must be directly transmitted to the Office of Research Administration who will utilize this budget in its negotiations with the Sponsor.

(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 HHC. The PI 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 HHC 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 Costs¹³⁰ and regarding Routine Costs in Clinical Trials.¹³¹ 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.¹³²

(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.

31.3.3. Reconciliation of Payments. The Facility Financial Analyst should reconcile all payments to ensure that all payments due to HHC 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.

31.3.4. Education and Training. Office of Research Administration at Central Office and Facility Executive Director shall be responsible for ensuring that HHC policies concerning billing compliance are disseminated and understood.

31.3.5. Sanctions.

(a) Non-compliance with this Section 31 shall include, but is not limited to, the submission of incomplete, erroneous, or misleading billing. Non-compliance with this Section 31 will result in HHC 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 HHC's Employee Disciplinary Policy and/or Medical Staff By-Laws.

(c) Non-compliance with this Section 31 may also result in penalties levied against the departments, divisions, Affiliates and/or HHC.

SECTION 32. RESIDUAL BALANCE ON FIXED PRICE AWARDS AND SPONSOR CONTRACTS

32.1. Definitions

For purposes of this Section 32 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.

32.2. **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 HHC, the Facility, the PI 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.

32.3. **Procedure**

32.3.1. **Quarterly Distributions of Anticipated Overage.**

(a) Prior to the commencement of the Current Budget Period of a Fixed Price Grant, the PI, 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 PI 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 HHC’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 HHC's indirect costs.

32.3.2. Researcher Certified Statement. If there is a residual balance at the end of the Current Budget Period of a Fixed Price Grant, the PI, 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 PI 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.

32.3.3. Facility Finance Office Certified Statement. After performing the reconciliation pursuant to Section 32.3.1(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.

32.3.4. 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 RA Office 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 PI 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 PI, 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.

32.3.5. 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.

32.3.6. Uses of the Funds in Account for Research Project Residual Funds.

(a) The monies in the Designated Account are institutional funds. The PI 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 HHC, following the procedures outlined in Section 32.3.6(d) below.

(b) Notwithstanding the above, these funds can only be used for other-than-personal-services (OTPS) expenditures, except as provided in Section 32.3.6(c), below, and may not be utilize for any of the following:

(i) Salary, bonuses or salary raises or any other compensation to any researcher whether employed by HHC, 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 PI or Department as continuing medical education expenditures, or funding which is otherwise the direct obligation of an Affiliate of HHC 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 HHC has reimbursed an Affiliate pursuant to an agreement with such Affiliate.

(c) For clarity, subject to Section 32.3.8, 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 HHC.

(d) PI or Department Chair shall submit receipts and other evidence of completed payment as HHC 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 HHC and is not a prohibited expenditure listed in Section 32.3.6(b) above, the monies shall be released to the PI or the Department in a timely manner. Alternatively, the PI 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, HHC may offset such amount by any amounts in the Designated Account.

32.3.7. In the event that a PI resigns, retires, or is no longer affiliated with HHC for any reason, the amount in the Designated Account associated with that PI may not be paid to such PI and may be expended only by the relevant Department, or may be reassigned for use by another PI by the chair of such Department.

32.3.8. Where an agreement with an Affiliate requires the funding of personal services positions with Residual Balances, the Anticipated Overage Amount referenced in Section 32.3.1 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 PART VI32.3.6(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.

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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*

*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
be 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
Footnotes continued from last page
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’ 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 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.

[FR Doc. 79-12065 Filed 4-17-79; 8:45 am] BILLING CODE 4110-08-M



**HHC HUMAN SUBJECT RESEARCH Protections PROGRAM
POLICIES AND PROCEDURES**

EXHIBIT 2

FACILITY COMMITMENT FORM

The New York City Health and Hospitals Corporation (“HHC”) 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 HHC 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 HHC 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-l, 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.

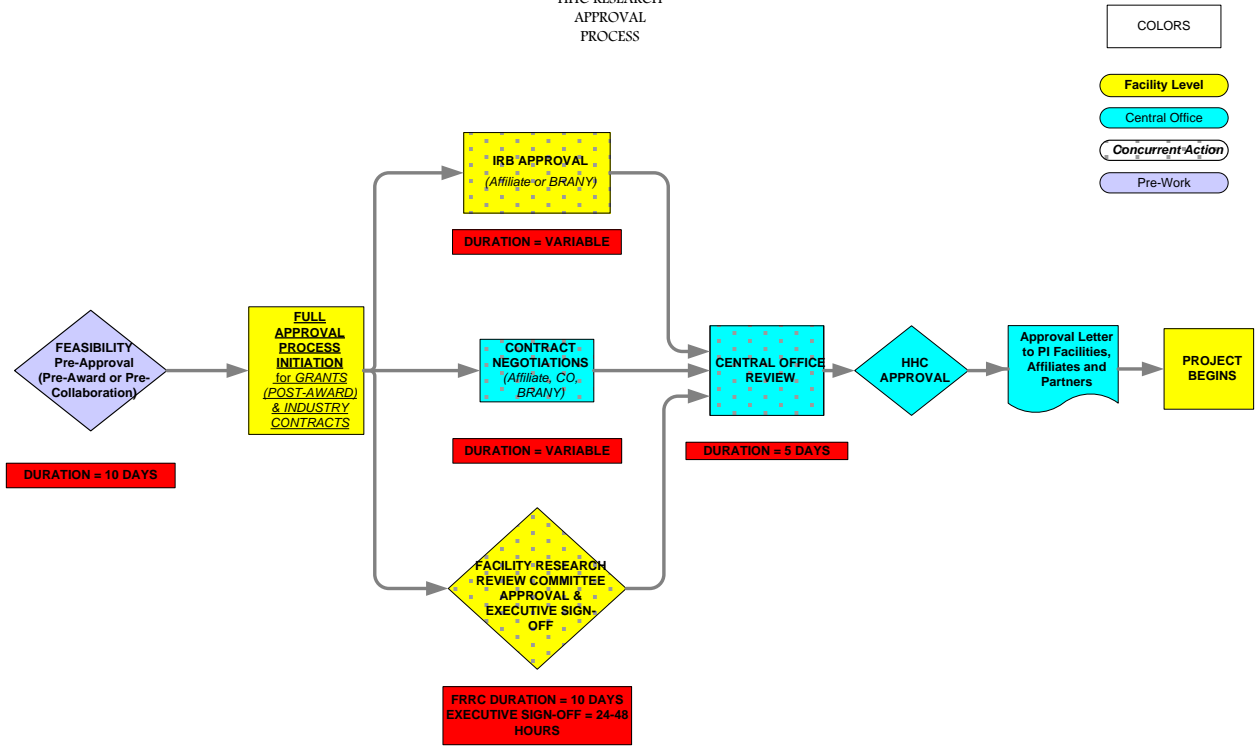
10 NYCRR § 405.7, patient rights with respect to human subject research.

New York Public Health Law Article 29-Cc (The Family Health Care Decisions Act).

EXHIBIT 4

PROCESS MAP

HHC RESEARCH
APPROVAL
PROCESS



V1 (HHC Fall 2011)

EXHIBIT 5

RESEARCH AGREEMENT REQUIRED CONTRACT PROVISIONS

The following provisions are required to be included in Research agreements. This is to provide PIs with a general understanding of what is acceptable to HHC to be in an agreement with a Sponsor. PIs should not rely on this information as a substitute for obtaining review by the RA Office and approval by OLA.

1. Confidentiality.

(a) HHC 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 HHC to disclose Research Project Data at any time as necessary for patient or public safety concerns.

2. Publication. HHC requires that all Research Project Data be freely publishable after a short period for review and comment by the Sponsor. 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 17 of this Policies and Procedure for more information.

3. Subject Injury. HHC's template subject injury language is as follows:

“Sponsor agrees that it, and not HHC, 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 HHC result from participation in the Study, except for such costs that arise directly from (i) the negligent activities, reckless misconduct or intentional misconduct of HHC, 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. HHC requires that ownership of all Inventions resides with HHC except for inventions resulting from Sponsor-authored Research Protocols.

5. Use of Name and Publicity. Use of HHC's name, logo, etc., for publicity or promotional purposes requires prior written consent.

EXHIBIT 6

GUIDANCE FOR LEGALLY AUTHORIZED REPRESENTATIVES ENROLLING DECISIONALLY INCAPACITATED INDIVIDUALS 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 7

**CONFLICT OF INTEREST FORM
DISCLOSURE OF SIGNIFICANT FINANCIAL INTERESTS AND OBLIGATIONS**

PART I

All HHC 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: _____

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 RA Office.

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 RA Office.

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 HHC Clinical Investigation & Research Policy 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):

- Consultant Employee
- Equity Interest Recipient of Honoraria
- Recipient of Royalties Travel
- Other (Describe): _____

3. The financial relationship is between the organization and (check all that apply):

- Self
- Spouse
- 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 8

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 HHC patients, facilities, staff or resources or which is conducted at an HHC 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	HHC	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 HHC 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 HHC 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 HHC may file.

VIIA. HHC Inventors:

Name of Primary Contact for HHC regarding this invention: _____

HHC Inventor Data (1)

Name:		Title:	
HHC Address:		Division:	
		HHC phone:	
e-mail:		HHC fax:	
Home Address:		Country of citizenship:	
Home phone:			

HHC Inventor Data (2)

Name:		Title:	
HHC Address:		Division:	
		HHC phone:	

e-mail:		HHC fax:	
Home Address:		Country of citizenship:	
Home phone:			

HHC Inventor Data (3)

Name:		Title:	
HHC Address:		Division:	
		HHC phone:	
e-mail:		HHC fax:	
Home Address:		Country of citizenship:	
Home phone:			

***Note: If there are more than three HHC inventors, please provide additional information on a supplemental sheet.**

VIIB. Non-HHC Inventors

Institution/Company/Organization	Non-HHC Inventor Name	Address/Email
None		

VIIC. HHC Inventor Signature(s): Per the HHC Research Policy, I (we) hereby disclose this invention to New York City Health and Hospitals Corporation (“HHC”) 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 HHC invention and hereby assign all rights, title and interests in and to this invention to HHC. I (we) further agree to execute all documents as requested to assign my (our) rights to HHC in and to any patent application or other statutory form of intellectual property protection filed in connection with this disclosure, and to cooperate with HHC's Office of Legal Affairs in securing protection of the disclosed invention.

I (We) do not believe this is a HHC invention as defined in HHC Research Policy and therefore should not be assigned to HHC. 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 HHC 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 HHC Office of Legal Affairs a written statement of all the reasons/justifications to support your request. HHC 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 9

INVESTIGATIONAL DRUG ACCOUNTABILITY LOG

Protocol Title: _____

Sponsor: _____

Principal Investigator: _____

Protocol Number: _____

IRB Number: _____

Drug Name, Dosage and Strength	Manufacturer or Supply Source	Date Received	Quantity Received	Expiration, Retest or Repass Date	Control, Lot, or ID Number	Human Subject Name or Identifier Receiving the Drug	Quantity Dispensed to Human Subject	Balance of Drug Remaining	Investigator Initials and Date

EXHIBIT 10

**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 (HHC) Affiliate”) and the HHC Medical Facility at _____ regarding the circumstances under which the HHC Affiliate agrees to provide study drug/device to the HHC 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 HHC Medical facility Pharmacy Service at _____ serves as a liaison between the HHC Affiliate and the HHC 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 HHC Affiliate and the Food and Drug Administration, when appropriate. The HHC 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 HHC Medical facility at _____ and the HHC Affiliate have agreed upon the following operating procedures in connection with the Study and this Letter of Understanding:

1. Conduct of the Study. The HHC Medical Facility at _____ will conduct the Study in accordance with the terms of Protocol and within HHC guidelines with the participation of the HHC Affiliate.
2. Drug Supply, Distribution, and Accountability. The HHC 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 HHC 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 HHC 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 HHC Affiliate.
3. Safety Information Reporting. The Principal Investigator is responsible for reporting adverse events with respect to Study Drug to the HHC 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 HHC 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 HHC Affiliate’s respective policies and procedures and regulatory reporting requirements. Accordingly, in the event of changes to HHC 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 HHC Affiliate. This is provided that the scope and extent of activity and undertakings are not materially increased. The HHC 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 HHC or the HHC 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 HHC policy. Reports issued for public distribution or to the HHC Affiliate will contain only aggregate data with all patient identifiers removed.

6. Selection of Participants. The HHC Medical Facility at _____ is responsible for all decisions concerning the selection and/or discontinuation of participants in the Study.

7. Record Retention. The HHC Medical Facility at _____ must retain all records related to the Study (according to HHC 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 HHC 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 PI) (Date)

(Name of the HHC Affiliate)

(Name and Signature of the HHC Facility CMO) (Date)

(Name of the HHC Facility)

EXHIBIT 11

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 (“HHC”) 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 HHC and HHC 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 HHC.
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 HHC for use by HHC 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. HHC have made, or may make Materials available to others, both profit and non-profit.

8. Recipient agrees to provide HHC with a copy of any publications which contain experimental results obtained from the use of the Materials. Recipient will acknowledge HHC as the source of the Materials in all publications and patent applications containing any data or information about the Material unless HHC indicates otherwise. HHC retains all right, title and interest in the trademarks registered or owned by HHC and any and all HHC catalog numbers or HHC specific designations of Materials.

9. Recipient shall notify HHC, in confidence, of any inventions that are conceived and reduced to practice through the use of the Materials (“Invention”). Recipient and HHC shall enter into good faith negotiations to negotiate a license with respect to any Invention Recipient will arrange the return to HHC 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. HHC MAKES NO REPRESENTATION AND PROVIDES NO WARRANTY 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 HHC an amount equal to any such tax(es), duties, tariffs and permit fees actually paid or required to be collected or paid by HHC and/or its designee.

(b) HHC 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, HHC will replace such Material at no additional charge, provided that you have reported lost or damaged shipments to the applicable carrier and notified HHC 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 HHC 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 HHC 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 12

INFORMED CONSENT FOR RESEARCH INVOLVING GENETIC TESTING

(The information below can be incorporated into a general consent, or be used as a separate consent along with a general consent. If necessary, translate into language of subject.)

Research Project Title:	Patient Name:
	Patient Address:
Research Project #:	
Principal Investigator:	

The New York City Health and Hospitals Corporation (HHC) 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 HHC, 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 HHC 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> The genetic test(s) will be done using the following sample: _____. The test(s) being ordered is/are _____. 	<input type="text"/>
<ul style="list-style-type: none"> <u>Purpose of the Test:</u> This testing is being conducted as part of the Research Project to determine: _____. <i>[Include a statement of the purpose of the test.]</i> 	<input type="text"/>
<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. 	<input type="text"/>
<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</i> 	<input type="text"/>

<i>sentence.]</i>	
<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 HHC for certain purposes:</u> You consent to HHC disclosing your results for your treatment purposes, to receive payment for services rendered to you and for HHC's operations relating to health care. 	<input type="text"/>
<input type="checkbox"/> I consent to genetic testing on my samples as part of the Research Project.	
<ul style="list-style-type: none"> • <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. <u>Please select one of the following:</u> 	<input type="text"/>
<ul style="list-style-type: none"> • <u>Use of Samples:</u> The samples that you give to HHC could one day lead to discoveries using methods and tests not yet developed. To that end, HHC 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>	
<input type="checkbox"/> Yes, I consent to the storage of the samples by HHC 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 HHC 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 HHC [or sponsor, if applicable] be destroyed. If you choose to do so, contact your study doctor, [name of PI], 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, HHC [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) HHC 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 HHC 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 HHC 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="1240 264 1362 317" 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> <ul style="list-style-type: none"> • <u>Test Results and Future Contact</u>: There may be circumstances in the future when HHC 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. 	<input data-bbox="1226 1100 1347 1152" type="checkbox"/>
<ul style="list-style-type: none"> • <u>Risks and Benefits of Future Contact</u>: HHC wants you to know that there may be both risks and benefits to consenting to future contact. <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="1226 1478 1347 1530" type="checkbox"/>

<p><input type="checkbox"/> 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><input type="checkbox"/> 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 OIG Compliance Guidance, available at <http://oig.hhs.gov/compliance/compliance-guidance/index.asp#top>.

² 45 C.F.R. § 46.501; <http://www.hhs.gov/ohrp/assurances/irb/>.

³ 21 C.F.R. § 56.106; <http://www.hhs.gov/ohrp/assurances/irb/>.

⁴ <http://www.hhs.gov/ohrp/policy/belmont.html>

⁵ 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>.

⁶ 45 C.F.R. § 46.116; 45 C.F.R. § 46.117

⁷ 45 C.F.R. § 46.103(b)(5)

⁸ 45 C.F.R. Part 46.

⁹ See Joint Commission Standard LD.01.03.01

¹⁰ A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information.

OHRP generally considers private information or specimens to be individually identifiable as defined at 45 C.F.R. § 46.102(f) 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.

¹¹ An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient.

¹² 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.

¹³ Please see HHC 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 HHC 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 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).

¹⁶ 45 C.F.R. § 46.116(c); 21 C.F.R. §§ 50.23 and 50.24; New York Public Health Law, Article 24-A, Section 2442.

¹⁷ 45 C.F.R. § 46.116.

¹⁸ 21 C.F.R. §§ 50.25 and 50.20.

¹⁹ Under 45 C.F.R. § 46.102(i) 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.”

²⁰ 45 C.F.R. § 46.11.

²¹ 45 C.F.R. § 46.117.

²² <http://www.fda.gov/regulatoryinformation/guidances/ucm126491.htm>.

²³ <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm>.

²⁴ 21 C.F.R. § 56.104(c) and 21 C.F.R. § 56.102(d).

²⁵ 21 C.F.R. § 50.24.

²⁶ 45 C.F.R. § 46.101(i).

²⁷ FDA requirements for legally effective Informed Consent are detailed in 21 C.F.R. §§ 50.20, 50.25 and 50.27.

²⁸ 21 C.F.R. § 50.23(a).

²⁹ NIH Guidelines for Research Involving Recombinant DNA Molecules, Section I-B, p. 10, available at http://osp.od.nih.gov/sites/default/files/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).

³⁰ NIH Guidelines for Research Involving Recombinant DNA Molecules, available at http://osp.od.nih.gov/sites/default/files/NIH_Guidelines.pdf.

³¹ CDC, *Biosafety in Microbiology and Biomedical Laboratories*, available at <http://www.cdc.gov/biosafety/publications/bmb15/BMBL.pdf>.

³² NIH and OBA *Frequently Asked Questions about Externally Administered Institutional Biosafety Committees (IBCs)*, available at http://osp.od.nih.gov/sites/default/files/resources/External_IBC_FAQs.pdf; NIH Guidelines for Research Involving Recombinant DNA Molecules, Section IV-B-1-c, p. 25, available at http://osp.od.nih.gov/sites/default/files/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).

³³ NIH Guidelines for Research Involving Recombinant DNA Molecules, at Section IV-B-1-g and h, p. 25, available at http://osp.od.nih.gov/sites/default/files/NIH_Guidelines.pdf; 10 NYCRR 61-1.30(g).

³⁴ NIH Guidelines for Research Involving Recombinant DNA Molecules, at Section IV-B-2-a-(3), p. 27, available at http://osp.od.nih.gov/sites/default/files/NIH_Guidelines.pdf.

³⁵ N.Y. Pub. Health Law § 3222; 10 NYCRR 61-1.3(a).

³⁶ 10 NYCRR 61-1.33(c).

³⁷ NIH Guidelines for Research Involving Recombinant DNA Molecules, Appendix M-I-B, p. 102, available at http://osp.od.nih.gov/sites/default/files/NIH_Guidelines.pdf; 10 NYCRR 61-1.33(b).

³⁸ NIH Guidelines for Research Involving Recombinant DNA Molecules, at Appendix M, p. 99, available at http://osp.od.nih.gov/sites/default/files/NIH_Guidelines.pdf.

³⁹ NIH Guidelines for Research Involving Recombinant DNA Molecules, at Section IV-B-7-d and e, p. 31, available at http://osp.od.nih.gov/sites/default/files/NIH_Guidelines.pdf; 10 NYCRR 61-1.33(d) and (e).

⁴⁰ 45 C.F.R. §§ 46.401-46.408; 21 C.F.R. Part 50, Subpart D; Chapter 14, Domestic Relations Law, Article 1 §2.

⁴¹ 45 C.F.R. § 46.407.

⁴² 45 C.F.R. § 46.405-408.

⁴³ OHRP Research with Children – FAQs, available at <http://answers.hhs.gov/ohrp/categories/1570>.

⁴⁴ 45 C.F.R. § 46.409(a).

⁴⁵ 45 C.F.R. § 46.409(b).

⁴⁶ 45 C.F.R. § 46.408.

⁴⁷ 45 C.F.R. §§ 46.201-46.207.

⁴⁸ 45 C.F.R. §§ 46.305 and 46.306.

⁴⁹ <http://grants.nih.gov/grants/policy/hs/prisoners.htm>.

⁵⁰ 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.

⁵¹ NIH, *Research Involving Individuals with Questionable Capacity to Consent: Points to Consider*, (November 2009), <http://grants1.nih.gov/grants/policy/questionablecapacity.htm>; OHRP: Institutional Review

Board Guidebook, Chapter VI, Section D, *Cognitively Impaired Persons*, http://www.hhs.gov/ohrp/archive/irb/irb_chapter6.htm#g5; 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.

⁵² New York Public Health Law §2994-d(1).

⁵³ NYS Public Health Law § 2444(2).

⁵⁴ N.Y. Mental Hyg. Law § 33.13(c)(9)(iii).

⁵⁵ 14 NYCRR § 815.11.

⁵⁶ 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.

⁵⁷ 20 U.S.C. § 1232g; 34 C.F.R. Part 99.

⁵⁸ 20 U.S.C. § 1232h; 34 C.F.R. Part 98.

⁵⁹ 20 U.S.C. § 1232g(b).

⁶⁰ 20 U.S.C. § 1232h(a).

⁶¹ 20 U.S.C. § 1232h(b).

⁶² http://schools.nyc.gov/NR/rdonlyres/F1942EF6-CE3D-4A8D-AE56-6B709EC70265/0/Proposal_Guidelines_Revised2102012.pdf.

⁶³ 45 C.F.R. § 46.111(b).

⁶⁴ NIH Frequently Asked Questions, Certificates of Confidentiality, A.2, available at <http://grants.nih.gov/grants/policy/coc/faqs.htm>.

⁶⁵ 42 U.S.C. §241(d), Protection of privacy of individuals who are research subjects. *See also* OHRP Guidance on Certificates of Confidentiality, available at <http://www.hhs.gov/ohrp/policy/certconf.html>; NIH Office of Extramural Research, *Key Information about Certificates of Confidentiality For Institutional Officials*, available at http://grants.nih.gov/grants/policy/coc/keyinfo_officials.doc.

⁶⁶ NIH Frequently Asked Questions, Certificates of Confidentiality, B.2, available at <http://grants.nih.gov/grants/policy/coc/faqs.htm>.

⁶⁷ NIH Office of Extramural Research, Certificates of Confidentiality FAQs, available at <http://grants.nih.gov/grants/policy/coc/faqs.htm#365>.

⁶⁸ 42 USC 299c-3(c); DHHS Agency for Healthcare Research and Quality, Frequently Asked Questions, available at https://info.ahrq.gov/app/answers/detail/a_id/583/~/~is-a-certificate-of-confidentiality-necessary-for-my-ahrq-supported-research.

⁶⁹ DHHS National Instituted of Health, Grants and Funding Frequently Asked Questions, available at <http://grants.nih.gov/grants/policy/coc/faqs.htm##>.

⁷⁰ 21 C.F.R. Part 54.

⁷¹ 45 C.F.R. § 46.101(b).

⁷² OHRP Guidance on Withdrawal of Subjects from: Data Retention and Other Related Issues, available at <http://www.hhs.gov/ohrp/policy/subjectwithdrawal.html>.

⁷³ 42 U.S.C. Section 262.

⁷⁴ GCP Guidance, Sections 7.1 and 7.3.

⁷⁵ GCP Guidance, Section 5.18; 21 C.F.R. § 3.12.53(d).

⁷⁶ 21 C.F.R. Part 312; *Guidance for Industry, E6 Good Clinical Practice: Consolidated Guidance*, U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), April 1996 (the “GCP Guidance”), available at <https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=2&cad=rja&sqi=2&ved=0CEQQFjAB&url=http%3A%2F%2Fwww.fda.gov%2Fdownloads%2FDrugs%2FGuidances%2Fucm073122.pdf&ei=S8HeUbmEGsXuyQH4xoCQBQ&usq=AFQjCNEGM5z67uCI2oKWssWIWs8qt5zqTw&sig2=8PN0Y4c3sqwyoqQml8wPqA>; New York Public Health Law Article 33; 10 NYCRR 405.17(a)(2)(iii).

⁷⁷ 21 C.F.R. § 312.53(b); GCP Guidance, Section 5.14.

⁷⁸ GCP Guidance, Section 4.6.2.

⁷⁹ GCP Guidance, Section 4.2.3.

⁸⁰ GCP Guidance, Section 4.2.4; 10 NYCRR 405.17(a)(9).

⁸¹ GCP Guidance, Section 4.6.3; N.Y. Edu. Law § 6817(1)(a).

⁸² 21 C.F.R. § 312.62.

⁸³ 10 NYCRR 405.17(a)(6).

⁸⁴ 21 C.F.R. § 312.53(b).

⁸⁵ 10 NYCRR § 405.17(c)(2).

⁸⁶ 21 C.F.R. Part 11.

⁸⁷ 21 C.F.R. § 312.6(a).

⁸⁸ <http://www.usp.org/usp-healthcare-professionals/compounding/compounding-general-chapters>.

⁸⁹ 21 C.F.R. § 312.59.

⁹⁰ 10 NYCRR 405.17(b)(4).

⁹¹ Available at http://www.wadsworth.org/labcert/clep/ls_standards_current.htm.

- ⁹² Final NIH Genomic Data Sharing Policy, 79 Fed. Reg. 51345 (Aug. 28, 2014).
- ⁹³ N.Y. Civ. Rights Law § 79-L (2)(b)(7).
- ⁹⁴ N.Y. Civ. Rights Law § 79-L (2)(f).
- ⁹⁵ N.Y. Civ. Rights Law § 79-l(2)(b); Wadsworth Genetic Testing Standard 5, available at <http://www.wadsworth.org/labcert/clep/files/CytogeneticsGeneticTesting.pdf>.
- ⁹⁶ N.Y. Civ. Rights Law § 79-L (2)(f).
- ⁹⁷ N.Y. Civ. Rights Law § 79-l(4)(a).
- ⁹⁸ N.Y. Civ. Rights Law § 79-l (2)(c) and (9)(a); Wadsworth Genetic Testing Standard 1, available at <http://www.wadsworth.org/labcert/clep/files/CytogeneticsGeneticTesting.pdf>.
- ⁹⁹ N.Y. Civ. Rights Law § 79-l(9)(c).
- ¹⁰⁰ The Genetic Information Nondiscrimination Act, 42 U.S.C., Chapter 21F.
- ¹⁰¹ OHRP Guidance on the Genetic Information Nondiscrimination Act: Implications for Investigators and Institutional Review Boards, <http://www.hhs.gov/ohrp/policy/gina.pdf>.
- ¹⁰² N.Y. Civ. Rights Law § 79-1(3)(a) and (b), and (9)(d); Wadsworth Genetic Testing Standard 14, available at <http://www.wadsworth.org/labcert/clep/files/CytogeneticsGeneticTesting.pdf>.
- ¹⁰³ OHRP Guidance on the Genetic Information Nondiscrimination Act: Implications for Investigators and Institutional Review Boards, <http://www.hhs.gov/ohrp/policy/gina.pdf>.
- ¹⁰⁴ N.Y. Civ. Rights Law § 79-l(11); see also N.Y. Pub. Health Law § 4306(a) with regard to anatomical gifts and terms of use.
- ¹⁰⁵ 67 Fed. Reg. 53182, 53231.
- ¹⁰⁶ N.Y. Civ. Rights Law § 79-l(9)(b).
- ¹⁰⁷ N.Y. Civ. Rights Law § 79-l(10).
- ¹⁰⁸ N.Y. Pub. Health Law § 4300, *et seq.*
- ¹⁰⁹ N.Y. Pub. Health Law §§ 4302, 4303.
- ¹¹⁰ 42 C.F.R. §§ 93.309, 93.310(b).
- ¹¹¹ 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).
- ¹¹² See <http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm126572.pdf>.
- ¹¹³ 45 C.F.R. § 46.103(b)(4)(iii).

¹¹⁴ There are many acceptable definitions for Adverse Events. HHC 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 HHC PI initiated protocol, the above definition should be utilized.

¹¹⁵ 45 C.F.R. § 46.103(b)(5).

¹¹⁶ 45 C.F.R. § 46.103(a) and (b)(5).

¹¹⁷ 45 C.F.R. § 46.103(a) and (b)(5).

¹¹⁸ 10 NYCRR § 404.10(b); Section 482.24(c) STATE OPERATIONS MANUAL, Appendix A-Survey Protocol, Regulations and Interpretive Guidelines for Hospitals.

¹¹⁹ See, e.g. 21 CFR § 312.62 and 21 CFR 812.140.

¹²⁰ 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 (last accessed on October 28, 2014); 8 NYCRR § 29.2; *see also* 45 CFR § 164.528 (accounting for disclosures of identifiable health information made in the context of research).

¹²¹ 45 C.F.R. 46.115(b).

¹²² 45 C.F.R. Part 46.

¹²³ 8 NYCRR Part 185.

¹²⁴ 45 C.F.R. § 46.116(a)(6), 21 C.F.R. § 50.25(a)(6).

¹²⁵ NIH Grants Policy Statement, October 1, 2013, Section 19.2, Definitions.

¹²⁶ Medicare National Coverage Determinations Manual Section 310.1.

¹²⁷ NIH Grants Policy Statement, October 1, 2013, Section 19.2, Definitions.

¹²⁸ NIH Grants Policy Statement, October 1, 2013, Section 19.3, Policy.

¹²⁹ Centers for Medicare and Medicaid Services National Coverage Decision for Routine Costs of a Clinical Trial, July 9, 2007.

¹³⁰ NIH Grants Policy Statement, October 1, 2013.

¹³¹ 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.

¹³² 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; OMB Circular A-110.21(b)(3).