Human Research Protection Program

Plan

Revised November 13, 2018

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Scope

Throughout this document "Institution" refers to MedStar Health, including any hospital, facility, or entity owned or controlled by MedStar Health related to clinical and other research.

MedStar Health Research Institute (MHRI) is the executive agent for research and provides central business, technical, administrative, financial, and regulatory infrastructure for employees and agents conducting research across MedStar Health.

Purpose

This Institution is committed to protecting the rights and welfare of subjects in Human Research. The purpose of this plan is to describe this Institution's plan to comply with ethical and legal requirements for the conduct and oversight of Human Research.

This Institution's Human Research Protection Program is a comprehensive system to ensure the protection of the rights and welfare of subjects in Human Research. The Human Research Protection Program is based on all individuals in this Institution along with key individuals and committees fulfilling their roles and responsibilities described in this plan.

Jurisdiction of the MedStar Health Human Research Protection Program (HRPP)

The HRPP jurisdiction extends to all research (funded and unfunded) involving human subjects conducted at MedStar Health by MedStar Health employees, faculty and students, as well as research conducted elsewhere by MedStar Health employees, faculty, and students, excluding research where involvement of human subjects falls within one or more exempt categories. This jurisdiction is effective regardless of the IRB of record reviewing the research study.

Definitions

Agent

An individual who is an employee is considered an agent of this Institution for purposes of engagement in Human Research when that individual is on-duty in any capacity as an employee of this Institution.

An individual who is not an employee is considered an agent of this Institution for purposes of engagement in Human Research when that individual has been specifically authorized to conduct Human Research on behalf of this Institution.

Legal counsel has the ultimate authority to determine whether someone is acting as an agent of this Institution.

Clinical Trial

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

Engaged in Research

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

- Intervention for research purposes with any human subjects of the research by performing invasive or noninvasive procedures.
- Intervention for research purposes with any human subject of the research by manipulating the environment.
- Interaction for research purposes with any human subject of the research.
- Obtaining the informed consent of human subjects for the research.
- Obtaining for research purposes identifiable private information or identifiable biological specimens from any source for the research. In general, obtaining identifiable private information or identifiable specimens includes, but is not limited to:

  observing or recording private behavior;
  using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided by another institution; and
  using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.

More information on engagement can be found at:
http://www.hhs.gov/ohrp/policy/engage08.html

Experimental Subject (DoD funded research only)

For investigators doing research funded by the Department of Defense, experimental subject is defined as subjects included in an activity, for research purposes, where there is intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. This definition does not include research involving the collection or study of existing data, documents, records, or specimens from living individuals.

Human Research:

Any activity that either:

- Is “Research” as defined by DHHS and involves “Human Subjects” as defined by DHHS (“DHHS Human Research”); or
- Is “Research” as defined by FDA and involves “Human Subjects” as defined by FDA (“FDA Human Research”).

Human Subject as Defined by DHHS

A living individual about whom an investigator (whether professional or student) conducting research (1) obtains information or biospecimens through Intervention or Interaction with the individual, and uses studies, or analyzes the information or biospecimens, or (2) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. For the purpose of this definition:

- **Intervention** means both physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- **Interaction** means communication or interpersonal contact between investigator and subject.
- **Private Information** means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (for example, a medical record).
- **Identifiable Private Information** means private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
- **Identifiable Biospecimen** means a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

Human Subject as Defined by FDA

An individual who is or becomes a subject 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. A human subject includes an individual on whose specimen (identified or unidentified) a medical device is used.

Investigator

The person responsible for the conduct of the Human Research at one or more sites. If the Human Research is conducted by a team of individuals at a trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

Research as Defined by DHHS

A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.[1]

Research as Defined by FDA

Any experiment that involves a test article and one or more human subjects, and that meets any one of the following:

[1] For research conducted within the Bureau of Prisons: Implementation of Bureau programmatic or operational initiatives made through pilot projects is not considered to be research.

- Must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act meaning any use of a drug other than the use of an approved drug in the course of medical practice;
- Must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act meaning any activity that evaluates the safety or effectiveness of a device; OR
- Any activity the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

Mission

The mission of this Institution's Human Research protection program plan is to protect the rights and welfare of subjects involved in Human Research that is overseen by this Institution.

Ethical Requirements

In the oversight of all Human Research, this Institution (including its investigators, research staff, students involved with the conduct of Human Research, the Institution's institutional review boards (IRBs), IRB members and chairs, IRB staff, the Institutional Official, and employees) follows the ethical principles outlined in the April 18, 1979 report of The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research titled "Ethical Principles and Guidelines for the Protection of Human Subjects of Research," also known as "The Belmont Report":

- Respect for Persons
- Beneficence
- Justice

Legal Requirements

All Human Research must undergo review by one of the institutionally designated IRBs. Activities that do not meet the definition of Human Research do not require review and approval by one of the Institution's IRBs and do not need to be submitted to one of the Institution's IRBs Any questions about whether an activity meets the regulatory definitions of Human Research should be referred to the Office of Research Integrity (ORI) who will provide a determination.

Common Rule (Federal Sponsors)

When this Institution is engaged in Human Research that is **conducted, funded, or otherwise subject to regulations by a federal department or agency** who is a signatory of the Common Rule, the Institution commits to apply the regulations of that agency relevant to the protection of Human Subjects as promulgated in 45CF46 in addition to any agency specific requirements.

FDA

When this Institution is engaged in **FDA regulated human subject research**, this Institution commits to apply the FDA regulations relevant to the Protection of Human Subjects codified in 21 CFR50 (Protection of Human Subjects) and 21 CFR 56 (Institutional Review Boards), Additional regulations that are relevant to IRB review of research are Parts 11 (electronic records), 312 (Investigational New Drug Application), 600 (Biological products), 812 (Investigational Device Exemptions), and 860 (Medical Device Classification Procedures). FDA regulations are largely congruent with DHHS regulations. However, some differences do exist.

Department of Defense

When Human Research is conducted or funded by the **Department of Defense (DOD**), this Institution commits to apply the Department of Defense (DOD) Directive 3216.02, which includes the requirement to apply 45 CFR §46 Subparts B, C, and D[2]. This Institution will comply with the terms of the DFARS clause or comparable language used in the agreement with the Department of Defense (DOD) Component supporting the research involving human subjects.

Department of Education

When Human Research is conducted or funded by the **Department of Education (ED**), this Institution commits to applying 34 CFR §97 Subpart D (equivalent to 45 CFR §46 Subpart D), 34 CFR §98.3, 34 CFR §98.4, 34 CFR §356.3, and 34 CFR §99.

Department of Energy

When Human Research is conducted or funded by the **Department of Energy (DOE),** this Institution commits to applying the Department of Energy (DOE) O 443.1B and to use "DOE Institutional Review Board Template for Reviewing Human Subjects Research Protocol that Utilize Personally Identifiable Information (PII)."

Environmental Protection Agency

When Human Research is conducted or funded by, or when the results of research are intended to be submitted to or held for inspection by the **Environmental Protection Agency (EPA**), this Institution commits to applying 40 CFR §26, which includes the requirement to apply 45 CFR §46 Subparts B and D.

[2] Quick applicability table for DHHS Subparts:

	DHHS	DOD	ED	EPA	VA
Subpart B	X	X		X	
Subpart C	X	X			X
Subpart D	X	X	X	X	X

Other Requirements

Community Based Participatory Research

Community Based Participatory Research (CBPR) is research that engages communities as active partners and collaborators with an institution. Where appropriate, the role of the community members in the research process includes the design and implementation of research and the dissemination of results. When reviewing research that involves community based research, the IRB obtains consultation for advice and knowledge on the research in the community and provides training to community based research team members.

International Research

When an investigator collaborates with or plans to study subjects in a foreign country, additional requirements may need to be satisfied. Care must be taken to ensure that the cultural norms of the host country are respected and that the participants will not suffer adverse consequences from participation, such as being subjected to retaliation from local authorities or the local community. If the country of collaboration or investigation has regulations to protect human subjects, then at a minimum they must be met in addition to local, state and federal regulations. If no regulations are in place, then the investigator should apply all policies and procedures identically to all research regardless of whether the research is conducted domestically or in another country, including:

- Confirming the qualifications of investigators for conducting the research
- Conducting initial review, continuing review, and review of modifications to previously approved research
- Handling complaints, non-compliance, and unanticipated problems involving risks to subjects or others
- Consent process and other language issues
- Ensuring all necessary approvals are met
- Coordination and communication with local IRBs or other regulatory bodies

Good Clinical Practice

For clinical trials, this Institution commits to apply the "International Conference on Harmonisation – Good Clinical Practice E6" (ICH-GCP).

Referrals

This Institution prohibits payments to professionals in exchange for referrals of potential subjects ("finder's fees") and payments designed to accelerate recruitment that were tied to the rate or timing of enrollment ("bonus payments.")

Human Research Protection Program Policies and Procedures

Policies and procedures for the Human Research Protection Program are available on the following intranet site:
http://starport.medstar.net/MHRI/policies/MHRI%20Policies/Forms/By%20Section.aspx.

Human Research Protection Program (HRPP) Components

The Institution has established a system wide Human Research Protection Program (HRPP) to oversee research conducted with human subjects. The team is comprised of the President of MHRI, staff in the Office of Research Compliance, staff in the ORI, staff in the Office of Grant and Contract Management and MHRI Institutional Review Board (IRB) with reliance agreements in place to rely on other authorized external IRBs.

All faculty, students and staff who wish to conduct research with human subjects at any MedStar Health owned or sponsored facility must obtain appropriate institutional ***and*** IRB approval before undertaking such research. No research with human subjects may commence without the approval of an authorized Institutional Review Board (IRB).

MedStar Health has a Federal Wide Assurance (FWA) to cover all of its facilities, which assures the Department of Health and Human Services (DHHS) that it will follow procedures to assure the protection of all human subjects involved in research projects. The assurance is a formal agreement between the Office for Human Research Protections (OHRP) and the authorized Institutional Official for the institution. This assurance applies to all research involving human subjects regardless of source of funding or support conducted at the institution, as well as to research conducted elsewhere by physicians, students, staff, or other representatives of the institution in connection with their institutional responsibilities.

It is the responsibility of the Institutional Official to oversee compliance with federal regulations related to human subject's research, at each institution. The Institutional Official holds signatory authority for all regulatory documents submitted to the Department of Health and Human Services and the Office for Human Research Protections. The Institutional Official maintains ultimate responsibility for complaints or concerns about the human research practices conducted within the institution. In addition, on an annual basis the Institutional Official reviews the budget and assures that the HRPP has sufficient resources.

The following outlines some specific roles and responsibilities of HRPP Components.

Institutional Official

The President of MedStar Health Research Institute is designated as the Institutional Official (IO). The Institutional Official has the authority to take the following actions or may delegate these authorities to a designee:

- Establish and allocate resources to Human Research Protection Program
- Appoint and remove MHRI IRB members and MHRI IRB chairs.
- Establish the MHRI IRB and authorize which IRBs the Institution will rely upon
- Place limitations or conditions on an investigator's or research staff's privilege to conduct Human Research.
- Suspend, disapprove or terminate research at MedStar Health approved by one of the Institution's authorized IRBs.

The Institutional Official has the responsibility to:

- Oversee the Human Research Protection Program.
- Ensure that the Human Research Protection Program has sufficient resources, including IRBs appropriate for the volume and types of Human Research to be reviewed, so that reviews are accomplished in a thorough and timely manner.
- Ensure that the research review process is independent and free of coercion or undue influence, and ensure that officials of the Institution do not approve research that has not been approved by one of the IRBs designated by the Institution.
- Enforce institutional policies
- Fulfill educational requirements mandated by OHRP.
- Review and sign federal assurances (FWA) and addenda.
- Periodically review this plan to assess whether it is providing the desired results and recommend amendments as needed.

Office of Research Integrity

The Office of Research Integrity (ORI) is the central business office that supports the operations and functions of the Human Research Protection Program (HRPP). The ORI provides this support through:

- Management of Regulatory Committees including the MHRI IRB
- Management of the IRB reliance process
- Management of the electronic IRB system and maintains applicable records
- Implementation of a process to receive and act on complaints and allegations regarding the Human Research Protection Program.
- Follow-up on findings of serious or continuing non-compliance
- Establishment and implementation of policies and procedures designed to increase the likelihood that Human Research will be conducted in accordance with ethical and legal requirement.
- Development and implementation of regular, effective, educational and training programs for all individuals involved with the Human Research Protection Program.

Research Compliance

The Research Compliance program, administered by the Office of Corporate Business Integrity, promotes and supports ethical research practices across the MedStar Health System. The Research Compliance program serves the MedStar research community by

- Coordinating system-wide research compliance policy and procedure development,
- Ensuring MedStar investigators are compliant with federal, state, and local laws and regulations, as well as MedStar policies.
- Administering the conflict of interest process for research.
- Oversees HIPAA in the context of research at MedStar

The Research Compliance Director

- Oversees the quality assurance program, which conducts routine and for cause audits of human subjects research at MedStar Health.

- Serves as the Research Integrity Officer, investigating allegations of scientific misconduct in research.
- Serves the Privacy Officer for research at MedStar Health and should be consulted on issues of HIPAA compliance.
- Serves as a regulatory resource to the Office of Research Integrity and the Institutional Review Board.
- Consults on issues of investigator noncompliance and noncompliance on the part of regulatory review committees and advises the Office of Research Integrity and the institution on appropriate resolution of identified concerns, including potential reporting to appropriate regulatory agencies.

The Office of Corporate Business Integrity Maintains the MedStar Integrity Hotline for reporting anonymous or confidential reports of activities that may involve unethical or otherwise inappropriate activity or behavior in violation of MedStar's established policies or local, state, or federal law

Members of the Institution

All individuals within the Institution have the responsibility to:

- Be aware of the definition of Human Research.
- Consult the IRB or ORI when there is uncertainty about whether an activity is Human Research.
- Not conduct Human Research or allow Human Research to be conducted without review and approval by an IRB authorized in writing through execution of an IRB Authorization Agreement or other similar document.
- Report allegations of undue influence regarding the oversight of the Human Research Protection Program or concerns about the Human Research Protection Program to ORI, Research Compliance or the Institutional Official.
- Report allegations or finding of non-compliance with the requirements of the Human Research Protection Program to the ORI, Research Compliance or the Institutional Official.

Institutional Review Boards

MHRI monitors all research involving human subjects at the Institution under the jurisdiction of its FWA. The Federal Wide Assurance number for MedStar Health is FWA # FWA00000504

Before a research project involving human subjects is initiated, it must first be reviewed and approved by a MHRI authorized IRB, This includes all research involving human subjects. In accordance with federal and state regulations governing research, an IRB must review and approve research involving human subjects prior to its initiation. It is the responsibility of the IRB to determine whether proposed research exposes subjects to unreasonable or unnecessary risk, to review informed consent forms and process, and to monitor the progress of research.

The safety, rights and welfare of human subjects is the most important consideration in the review of human subjects research protocols.

MHRI Institutional Review Board
The MHRI Institutional Review Board (IRB) is a committee whose purpose is to ensure that the rights and welfare of human subjects are protected in all medical, behavioral and social sciences research. The MHRI IRB is comprised of Committees with a designated IRB Chair and Vice-Chair. The ORI Director reviews the activity of the IRB on an annual basis to assure that the number of boards and meetings held is appropriate in relation to the activity of the Committees. This information is provided to the IO who decides whether to increase the number of committees or meetings.

Authority of the IRB
The IRB holds the authority to review, approve, require modifications in, place restrictions on, disapprove or suspend all research activities involving human subjects, including proposed changes in previously approved research, regardless of funding source and performance site, if the research is being conducted under the auspices of this institution and submitted to an authorized IRB for review.

Research that has been approved by the IRB may be subject to further appropriate review and approval or disapproval by officials of the institution or facility where the research is occurring. However, these officials may not approve research that has been disapproved by an authorized IRB. The decision of the IRB to disapprove a research study cannot be overturned by an external body, Institutional official or other individual.

The IRB shall have the further authority to:

- Request progress reports for a particular protocol at intervals defined by the IRB.
- Suspend or terminate approval of research that is not conducted in accordance with the IRB's requirements or that has been associated with unexpected harm to subjects.
- Review the credentials of investigators to ensure that they have the appropriate expertise to conduct the study properly.
- Impose additional conditions, which the full committee deems necessary for the protection of human subjects.
- Promulgate policies and procedures as necessary for the proper protection of human subjects.
- Observe or have a third party observe the consent process and the research, or monitor the research to ensure compliance.

Reliance on an IRB other than the MHRI IRB & IRB Authorization Agreements
When collaborating with other institutions, sometimes a single or joint IRB review may be preferred over separate reviews at each institution. The institution can enter into an IRB authorization agreement with other institutions, a Central IRB, and/or Independent IRB with whom the institution and employees collaborate on single or multiple projects.

When collaborating with other institutions, an IRB authorization agreement must is drafted. The IRB Authorization Agreement establishes a written understanding defining the scope of

responsibility of the respective institutions for the research study in which both institutions are involved in the review, approval and continuing oversight performed by the approving institutions IRB and the requirements of the HHS regulations for the protection of human subjects at 45CFR46 as well as the requirements of the federal, state and local laws. For research involving FDA regulated products the approving institution's IRB must be in compliance with requirements defined in 21 CFR Pats 50,56, 312 and 812.

This institution will comply with the determinations of the reviewing IRB, follow reporting and conflict of interest disclosure requirements as specified in the authorization agreement, conduct monitoring, identify an appropriate contact person, ensure researchers have appropriate qualifications and provide local context information (and any updates) to the reviewing IRB.

When this institution provides IRB review for other institutions, this HRPP will follow established policies and procedures to ensure that the composition of the IRB is appropriate to review the research and will comply with applicable laws of the relying site. This includes ensuring the IRB is appropriately constituted, members are appropriately qualified, members will not participate in the review of research in which they have a conflict of interest; and that the IRB separates business functions from ethical review.

Investigators and Research Staff

The PI of a research study at MedStar Health is the individual responsible for supervising and conducting the research. Investigators and research staff have the responsibility to:

- Follow the Human Research Protection Program requirements described in the INVESTIGATOR MANUAL (HRP-103).
- Comply with all determinations and additional requirements of the IRB, the IRB chair, and the Institutional Official.

Legal Counsel

Legal Counsel has the responsibility to:

- Provide advice upon request to the Institutional Official, IRB, and other individuals involved with the Human Research Protection Program.
- Determine whether someone is acting as an agent of the Institution.
- Determine who meets the definition of "legally authorized representative" and "children" when Human Research is conducted in jurisdictions not covered by policies and procedures.
- Resolve conflicts among applicable laws.

Department Chairs/Medical Directors/VP Medical Affairs

Department Chairs/Medical Directors/VP Medical Affairs have the responsibility to:

- Oversee the review and conduct of Human Research in their in their respective clinical area (e.g. department, clinical service line, clinical facility or hospital).
- Forward complaints and allegations regarding the Human Research Protection Program to the Institutional Official.

- Ensure that each Human Research study conducted in their respective clinical areas has adequate resources.

Office of Contract and Grant Management

The Office of Contract and Grant Management has the responsibility to review contracts and funding agreements for compliance with Human Research Protection Program policies and procedures.

Education and Training

All new employees engaged in human research are to review this plan as part of initial orientation.

IRB members, IRB staff, and others involved in the review of Human Research, including the Institutional Official, must complete initial and continuing training.

Investigators and research staff must complete the initial and continuing training described in the INVESTIGATOR MANUAL (HRP-103).

Questions and Additional Information for the IRB

The ORI wants your questions, information, and feedback. Contact and location information for the ORI is:

Director, Office of Research Integrity
6525 Belcrest Rd.
Suite 700
Hyatsville, MD 20782
orihelpdes@medstar.net
301-560-7300

Reporting and Management of Concerns

Questions, concerns, complaints, allegations of undue influence, allegations or findings of non-compliance, or input regarding the Human Research Protection Program may be reported orally or in writing. Employees are permitted to report concerns on an anonymous basis. Concerns may be reported to the IRB Chair, ORI, Institutional Official, the Research Compliance Director, Legal Counsel, Department Chairs.

The IRB has the responsibility to investigate allegations and findings of non-compliance and take corrective actions as needed. The Institutional Official has the responsibility to investigate all other reports and take corrective actions as needed.

To make such reports, contact the Institutional Official:

Neil J. Weissman, MD
President, MedStar Health Research Institute

Professor of Medicine, Georgetown University
100 Irving St., Northwest
Suite EB-5123
Washington, DC 20010
Email: neil.j.weissman@medstar.net
(202) 877-0223

Employees who report in good faith possible compliance issues should not be subjected to retaliation or harassment as a result of the reporting. Concerns about possible retaliation should be immediately reported to the Office of Corporate Business Integrity. The Office of Corporate Business Integrity maintains the MedStar Integrity Hotline for reporting anonymous or confidential reports of activities that may involve unethical or otherwise inappropriate activity or behavior in violation of MedStar's established policies or local, state, or federal law. The hotline # is 1-877-811-3411.

Monitoring and Auditing

In order to monitor and ensure compliance, internal or external auditors who have expertise in federal and state statutes, regulations and institutional requirements will conduct periodic audits. Audits will focus on areas of concern that have been identified by any entity, i.e., federal, state or institutional. Random audits may also be conducted.

Disciplinary Actions

The Institutional Official may place limitations or conditions on an investigator's or research staff's privilege to conduct Human Research whenever in the opinion of the Institutional Official such actions are required to maintain the Human Research Protection Program.

Approval and Revisions to the Plan

This Human Research Protection Program Plan is to be approved by the Institutional Official. This plan is intended to be flexible and readily adaptable to changes in regulatory requirements. The Institutional Official has the responsibility to review this plan to assess whether it is providing the desired results.

Approved:
Neil J. Weissman, MD
President
November 13, 2018