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Title	Human Research Protections Program (HRPP)
Scope	North Memorial Health, Maple Grove Hospital, Blaze Health
Responsibility	North Memorial Health Research Office

PURPOSE

This Standard Operating Procedure (SOP) establishes the ethical principles, regulations, and general requirements for human subjects research conducted by Organization employees or trainees, in Organization facilities, or using Organization resources.

DEFINITIONS

Human subject (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**: 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**: Communication or interpersonal contact between Investigator and subject.
- **Private Information**: 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).
- **Sensitive Personally Identifiable Information (SPII):** Information that if lost, compromised or disclosed could result in substantial harm, embarrassment, inconvenience, or unfairness to an individual.
- **Identifiable Private Information**: Private Information for which the identity of the subject is or may readily be ascertained by the Investigator or associated with the information. NMH utilizes the eighteen (18) identifiers in the HIPAA Privacy Rule to determine whether data or biospecimens are identifiable.
- **Identifiable Biospecimen**: A biospecimen for which the identity of the subject is or may be readily ascertained by the Investigator or associated with the biospecimen. The Organization utilizes the 18 identifiers in the HIPAA Privacy Rule to determine whether data or biospecimens are identifiable.

Human subject (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 a medical device is used.

Institutional Official (IO): The individual who is legally authorized to act for the Organization and, on behalf of the Organization, obligates the Organization to the terms of its Federalwide Assurance (FWA). The IO is responsible for ensuring that the Human Research Protection Program (HRPP) functions effectively and that the Organization provides the resources and support necessary to comply with all requirements applicable to research involving human subjects. The IO represents the institution named in the FWA.

Reliance Agreement: Also called an Authorization Agreement, is the agreement that documents respective authorities, roles, responsibilities, and communication between an Institutional Review Board (IRB) providing the ethical review of human subjects research and the institution relying on the ethical review.

Research (HHS): A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. The following activities are deemed not to be research under the revised Common Rule (45 CFR 46):

- Scholarly and journalistic activities (oral histories, journalism, biographies, legal research and historical scholarship).
- Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority.
- Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
- Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

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

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

POLICY

The Organization's Human Research Protection Program (HRPP) is an integrated program of offices, oversight functions, education, quality assurance, researchers and research staff that together are responsible for protecting the rights, safety, and welfare of human subjects participating in research and ensuring compliance with applicable regulations and policies. The HRPP serves to promote excellence and ensure compliance in all aspects of human subjects

research and provides support for Organization researchers and research participants.

The Organization does not maintain its own IRB and relies on external IRBs for all non-exempt research and exempt research that requires limited IRB review.

Components of the HRPP

Institutional Official: The Organization's Chief Medical Officer serves as the Institutional Official (IO) and bears overall responsibility for the HRPP. The IO understands the Organization's responsibilities under the Federalwide Assurance (FWA) and ensures that the reviewing IRB is the only entity that can grant approval for non-exempt human subjects research. The IO ensures that no one within the Organization may approve non-exempt human subjects research that has not been approved by an IRB. However, the IO does have the authority to disapprove research that has been approved by an IRB. The IO is responsible for:

- Establishing and maintaining offices and workflows within the Organization to review and oversee human subjects research and ensure the protection of research participants;
- Adopting and enforcing written policies and procedures governing the conduct of human subjects research at the Organization or by Organizational employees (e.g., in a setting outside of an Organization facility);
- Implementing and maintaining an education program to ensure that members of the Organization's research community, including investigators, research staff, research administrators and other individuals who may support research at the Organization, understand the legal and ethical standards and regulations and policies under which human subjects research is conducted;
- Communicating with federal agencies including the Office of Human Research Protections (OHRP) and the Food and Drug Administration (FDA) when necessary; and
- Ensuring the HRPP has the resources, including staffing and budget, sufficient to ensure protection of the rights, safety, and welfare of participants.

Investigators and Research Staff: Investigators and research staff are a critical component of the HRPP and are the primary individuals responsible for ensuring protection of participants. Investigators and research staff members must be qualified by training and experience to conduct human subjects research and must comply with ethical principles, Organization policies regarding human subjects research, policies of the reviewing IRB, and federal regulations, as applicable.

Principal Investigators (PIs) may delegate responsibility for conducting certain research activities to co-investigators and research staff who are qualified by training and experience. However, the PI remains responsible for delegated tasks and for the overall conduct of the research.

North Memorial Health Research Office: The Research Office is responsible for administering the HRPP and for ethical and regulatory oversight of Organization human subjects research. The Research Office administers, supports, and guides the components of the HRPP to ensure that they work as a cohesive unit to protect the rights, safety, and welfare of participants. The Research Office also serves as a resource to investigators regarding regulatory questions, Organization policies, and education. The Research Office is responsible for:

- Developing, implementing, managing, and regularly evaluating policies related to human subjects research to ensure compliance with state and federal regulations;
- Advising the IO on key matters regarding Organization human subjects research;
- Conducting training and education for investigators, research staff, and the research community at large and ensuring that investigators have completed required training before engaging in human subjects research;
- Reviewing exempt human subjects research and issuing exempt determinations;
- Reviewing and approving requests to cede review of non-exempt research and exempt research requiring limited review, to an external IRB;
- Serving as the primary contact and liaison with external IRBs that are reviewing and providing oversight for Organization human subjects research;
- Serving as the Organization's subject matter expert on human subjects research;
- Maintaining appropriate documentation regarding Organization research, including records regarding exempt determinations, COI disclosures, and waivers/alterations of HIPAA authorization;
- Maintaining the Organization's Federalwide Assurance (FWA) with OHRP; and
- Overseeing day-to-day operations of the HRPP, which may include supervising staff.

Office of General Counsel: The Organization's Office of General Counsel interprets state law and conflicts of laws and is responsible for reviewing research related agreements including, but not limited to, clinical trial agreements, IRB reliance (authorization agreements), and Data Use Agreements (for use/disclosure of Limited Data Sets).

Radiation Safety: The Radiation Safety Committee reviews research protocols involving the use of ionizing radiation or radiopharmaceuticals for research purposes.

Investigational Pharmacy: The Investigational Pharmacy ensures the proper receipt, storage, dispensing, transfer, and disposal of investigational drugs and biologics.

Ethical Principles

As specified in the Organization's FWA, the Organization adheres to the ethical principles for the protection of human subjects set forth in the Declaration of Helsinki and the Belmont Report. The three ethical principles set forth in the Belmont Report are respect for persons, beneficence, and justice.

1. Respect for persons: Individuals are to be treated as autonomous agents, and persons with diminished autonomy are entitled to protection.
2. Beneficence: Persons are treated ethically not only by making efforts to secure their well-being. Researchers must do no harm, while maximizing possible benefits and minimizing possible harms.
3. Justice: The benefits and burdens of research shall be distributed equally.

Federal Regulations

The Organization adheres to applicable federal regulations when conducting human subjects research.

Department of Health and Human Services (HHS) Regulations (45 CFR 46): The Organization holds a FWA with OHRP and operates in full compliance with 45 CFR 46, including its subparts, when applicable. For clarity, although the Organization applies 45 CFR 46 to all human subjects research, the Organization has opted to limit the application of its FWA to non-exempt human subjects research conducted or supported by Common Rule agencies.

Food and Drug Administration (FDA) Regulations: The Organization participates in clinical investigations that fall under the jurisdiction of the FDA. The Organization complies with FDA regulations found at 21 CFR 50, 21 CFR 312, 21 CFR 812 and 21 CFR 814.

Human Subjects Research Determinations

Federal regulations govern when an activity constitutes human subjects research. The responsibility for initially determining whether an activity constitutes human subjects research rests with the PI who bears primary responsibility for the proposed activity. The PI should make the determination based on the applicable definitions of "human subject" and "research" set forth herein.

However, the analysis of whether an activity represents human subjects research can be complex and nuanced. Investigators who make incorrect determinations will be held responsible. As such, when it is unclear whether a proposed activity constitutes human subjects research, investigators are encouraged to contact the North Memorial Health Research Office for a formal review and written determination regarding whether the proposed activity does or does not constitute human subjects research. Determinations from other entities may not be used/substituted for a determination from the Organization.

The following activities are not considered to be research. However, Organization investigators may still wish to obtain a formal written determination from the North Memorial Health Research Office to retain in their records and provide to publications in the event such documentation is requested.

- Quality improvement: Systematic and data-guided activities designed to bring about immediate improvements in health delivery in particular settings.
- Program evaluation: A systematic method for collecting, analyzing, and using information to answer questions about projects, policies, and programs, particularly about their effectiveness and efficiency.
- Case reports: Unsystematic clinical observations based on a single case. A case report states the outcome or response of a single patient to a diagnostic strategy or treatment.
- Case series: An unsystematic retrospective clinical observation about more than one patient case. A case series sometimes reports on a variety of different diagnostic or therapeutic approaches. Case series are not considered research provided that there are 5 or fewer cases. Case series with more than 5 cases must be submitted for a determination regarding whether the series meets the definition of human subjects research.

PROCEDURES

Investigators requesting a formal determination regarding whether a proposed activity

constitutes human subjects research must contact the North Memorial Health Research Office by email at Research.Office@northmemorial.com. Requests must include a copy of the NMH Human Subjects Research Determination Request Form.

Research Office staff will review requests for human subjects research determinations in accordance with applicable federal regulations and guidance. When an activity does not represent human subjects research, a written "non-human subjects research" (NHSR) determination will be sent to the PI. When an activity represents human subjects research, Research Office staff will communicate with the PI to provide guidance on obtaining an exempt determination or initiating the process to request to rely on an external IRB, as appropriate based on the nature of the research.

REFERENCES

45 CFR 46
21 CFR 50, 312, 812, 814
SOP – Exempt Research
SOP – North Memorial Health Reliance on an External IRB

TABLE OF REVISIONS

Date	Description of Changes