Children's Hospital and Health System
Administrative Policy and Procedure

This policy applies to the following entity(s):
☒ Children's Hospital and Health System

SUBJECT - Research: Conduct of Research on Human Subjects at Children's Hospital and Health System

The jurisdiction of the Children's Wisconsin's ("Children's") Human Research Protection Program ("HRPP") extends to all Research as defined by federal regulations including those promulgated by the Office of Human Research Protection (OHRP) and the Food and Drug Administration (FDA). The jurisdiction of the Children's HRPP also extends to Research as defined by the federal Health Insurance Portability and Accountability Act ("HIPAA"). Meeting exemption criteria under OHRP regulations does not automatically waive the requirement for HIPAA authorization and IRB review, as the designated Privacy Board, under HIPAA.

- The Children's HRPP has been granted the authority to oversee all research studies conducted at Children's entities and has the authority to designate the IRB of record for research that engages Children's.
- Prior to enrolling a human subject, research that engages Children's must be reviewed and approved by an appropriately delegated IRB of record unless the research has been deemed to meet exemption criteria.
- When the delegated IRB of record is not functioning as the Privacy Board, the Children's HRPP has a designated Children's Privacy Board to review and document HIPAA waiver determinations for all research studies requiring access to non-public information from patient health care records maintained by Children's and/or an affiliated institution, in accordance with HIPAA.
- Anyone conducting research at Children's is required to follow the Children's HRPP Standard Operating Procedures ("SOP") manual, which further outlines requirements for the conduct of research at Children's.

Regulatory Definitions:

Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. DHHS regulations, 45CFR46.102(l).

Clinical investigation means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

The term does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part. FDA regulations 21CFR56.102(c).

Human Subjects is defined in DHHS regulations, 45CFR46.102(e)(1) and FDA regulations 21CFR56.102(e).

POLICY

Children's Wisconsin is committed and required to adhere to federal, state and local laws and regulations for the conduct of research involving human subjects. Children's maintains a Federal wide Assurance (FWA) with the Department of Health and Human Services (DHHS) Office of Human Research Protections (OHRP) covering Children's legal entities. This policy pertains to the conduct of research at all Children's entities. Please refer to the related Children's HRPP SOP manual which outlines additional requirements.

All individuals engaged in the conduct of human subjects research at CW must have appropriate knowledge and expertise, meet applicable credentialing qualifications and competencies, and be trained and knowledgeable about human subjects protections. Training requirements are set forth in the CW HRPP SOP manual.

The CW HRPP relies on the professional standards as required by The Joint Commission. These standards assure that those conducting research involving clinical interventions are capable of maintaining patient care standards and oversight of the quality of care and treatment, and that services are rendered by practitioners privileged through the medical staff process or by those with ongoing demonstration of clinical skills and competencies.

WHO CAN SERVE AS PI AT CW?

1. To be the Principal Investigator ("PI") for a research study that engages Children's Wisconsin, the individual must be an active member of the CW Medical/Dental staff or be an employee of CW or Children's Hospital and Health System ("CHHS").

2. If the study involves clinical interventions or procedures or involves administration of drugs/biologics/devices outside the scope of practice of the PI, the PI may delegate to appropriately qualified sub-investigators (see below).

3. For multi-site studies (including studies being conducted at Froedtert Hospital, MCW, or Versiti), an appropriately qualified Children's local site PI must be selected that meets these policy requirements to serve as a Children's PI.

4. Students, residents, and fellows cannot serve as PI when conducting human subjects research at a CW site. The PI must be a CW medical/dental staff member or CW or CHHS employee and must actively supervise all research activities conducted by the students/residents/fellows.

REQUIREMENTS FOR ALL INVESTIGATORS

1. For other investigators who are not members of the CW medical/dental staff nor CW or CHHS employees, these individuals must have an appropriate CW medical/dental staff member or CW or CHHS employee serve as the PI for the study. All research activities must comply with the CHHS standards and regulatory requirements for safety and health, including the individuals acting within their scope of practice and approved competencies.

2. All members of the study team must act within their scope of practice for their position and/or licensure.

3. Only individuals who have an active appointment to the Medical Staff and clinical privileges to attend patients at CW may conduct clinical interventions or procedures as part of human subjects research at CW.

4. All research conducted in CW facilities that involve children, parents or staff must be reviewed and approved by an Institutional Review Board (IRB) designated by the CW HRPP. Investigators must have written final approval from the IRB of record before conducting any research activities. Conducting research without IRB approval is considered serious noncompliance with federal regulations and CW HRPP policies, and will be subject to disciplinary action, which may include suspension of Medical Staff privileges or termination of employment.

5. Investigators are required to adhere to all policies, procedures and guidance established by CW and the IRB of record regarding the initial and subsequent submission of research protocols for approval, including the submission of continuing reviews.

6. Investigators planning research involving CHHS employees or staff as subjects must review the research with the Director of Human Resources in order to determine the appropriateness of research for the targeted employee group. Confidentiality and communication surrounding the research also will be reviewed. A letter of support from the Director of Human Resources is required.

7. In order to maintain the scientific integrity of the research and the rights and welfare of human subjects, any potential conflicts of interest for the PI or any member of the research team must be disclosed to the CW HRPP at the time of protocol submission. Conflicts of interest include, but are not limited to: partial ownership of a sponsoring

company, stock in the company or financial profit by conducting the research. The Conflict of Interest Committee has the right to request and review the contract between the investigator and the sponsoring agency. Please refer to the CW HRPP SOP manual section on conflicts of interest disclosure for more information.

5. In many instances, the use of treatments, drugs and devices for research purposes may not be charged to third party payers. The PI is responsible for complying with all Centers for Medicare and Medicaid Services (CMS) policies regarding financial reimbursement for research-related treatments. Certain studies may require a formal coverage analysis and approval by CW Corporate Compliance to determine what services are covered and what services may not be billed to third party payers (see related policy Clinical Research Billing at CW).

   CW Corporate Compliance should be notified of any use of identifiable private health information used for research purposes via the IRB submission and review process.

6. Researchers must obtain written administrative approval from the CW clinic manager/director allowing the conduct of the study in the intended CW clinic space. Ancillary services may not set up methods and procedures which are not part of their existing line of services. If reference lab services are required, the investigator may send out those labs independently with no CW Lab involvement or charges, or may send them out through the CW Lab. CW Lab will apply the standard fee for send-outs and the research discount applied when billing the research study.

7. CW Pharmacy must review and provide written administrative approval for all investigational drug/biologic studies. The CW Pharmacy Director will determine where investigational drugs/biologics may be stored within the hospital. Any investigators storing and dispensing investigational drugs/biologics outside of the CW Pharmacy will comply with all applicable regulatory requirements.

8. Obtaining research consent and authorization: The PI is responsible for delegating the consent process to appropriately trained and qualified individuals, and for ensuring that the initial and ongoing process of informed consent is conducted in accordance with federal regulations (45CFR46.116; 46.117 and 21CFR50.25, 50.27) as well as requirements outlined in the CW HRPP SOP manual. Failure to obtain legally effective informed consent when required by the IRB is considered serious noncompliance. In addition, the PI is responsible for ensuring compliance with the HIPAA Privacy Rule requirements for research.

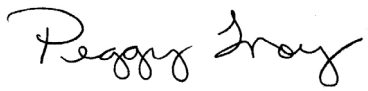
9. In situations where an FDA-approved device is being used as part of the study, the PI and study team must work with clinical engineering when introducing research equipment into CW space, and clearly describe in the protocol and submission materials the procedure for using the device, or reference the hospital policy regarding the use of

the device. The PI must ensure investigators/key personnel deploying the device are appropriately credentialed and operating within their scope of practice.

10. If CW is providing any service as part of the study protocol, or if any part of the study protocol is taking place in CW clinical space, the human subject must be registered as a CW patient. This includes human subjects who are seen only for research purposes. Human subjects completing questionnaires or dropping off samples do not need to be registered.

11. The PI must keep all relevant study documentation in accordance with the CW HRPP SOP manual and relevant CW policies. Copies of consent forms must be given or sent to the family. If documentation of informed consent/parental permission/assent/HIPAA authorization is required by the IRB, a copy of the signed consent, parental permission form, assent, and/or HIPAA authorization must be placed in the human subject's medical record if they are registered as patients at CW.

Approved by:



Peggy Troy, President & CEO
Children's Hospital and Health System
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