Is my project Human Subject Research?

Not every project falls within the purview of an IRB. There are research projects that are not human subject research, as well as projects that involve medical record review and/or interaction with patients that are considered quality improvement/operations rather than research. The scope of an IRB is limited to human subject research. Any project that meets this regulatory definition must be submitted to an IRB of approval and continuing oversite.

Differentiating can be tricky, and the CW HRPP office is available to discuss your project to help determine before any submissions what category may apply.

At Children's Wisconsin:

- There is not an institutional requirement to have a formal, written determination that an activity does not constitute human subject research. However, an investigator may want this documentation to provide to publishers or others if requested.
- CW does have a process to review and make this determination if needed.
- The Children's Wisconsin HRPP is the sole body at CW designated to make formal written determinations at Children's Wisconsin.
- Human Subjects Research Determinations must be submitted, and determined, prospectively (i.e. before the proposed activity or research begins).
- Conducting human subject research without IRB approval or exemption is noncompliance.

What is Research?

Research is defined in the Federal Regulations.

- The HHS definition is found at 45 CFR 46 102.7(l). *Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.*
- The FDA definition is found at 21 CFR 56.102(23)(c). The FDA has defined "clinical investigation" to be synonymous with "research". "*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 FDA…or 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.*

What is a human subject?

Research requires IRB review and approval when it involves human subjects. This is also defined by federal regulations.

HHS Regulations

- The HHS definition is found at 45 CFR 46 102.7(e)(1). *Human subject means a living individual about whom an investigator (whether professional or student) conducting research:(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or*
  (ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.
- These regulations further define:
  - Intervention: *Intervention includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.*
  - Interaction: *includes communication or interpersonal contact between investigator and subject.*
  - Private Information: *includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).*
  - 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.*
  - Identifiable Biospecimen: *a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.*

FDA Regulations

- The FDA definition is found at 21 CFR 56.102(23)(e). *Human subject means 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 individual or a patient.*

Decision tree – HHS

Human Subject Research Determinations

An activity will require IRB review if it determined to be both **research** and involves **human subjects. (see definitions above)** Except for some special types of projects (e.g., Expanded Access Humanitarian Use Devices), activities that do not meet the federal definitions of research and human subject do not require (as a matter of regulation) IRB review and oversight. *IRB Management and Function Chapter 5.*

The responsibility for initial determination of whether an activity constitutes "research" rests with the individual who has primary responsibility for the activity. This individual should make this determination based on the definitions of "research" and "clinical investigation" as provided by the Common Rule and U.S. Food and Drug Administration (FDA) regulations, respectively (see definitions). Consultation with the CW HRPP Office is encouraged.

Activities that are not human subject research under the Common Rule:

There are select activities that have been deemed not to be research under the revised Common Rule. As long as all conditions are met, these four activities are deemed to not be research. (45 CFR 46.102(1)(1-4)

- Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focuses directly on the specific individuals about whom the information is collected.
- 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 investigation purposes.
- Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

Quality Improvement v. Research

- At times it may be difficult to discern whether a proposed activity constitutes research or human subject research, quality improvement or an operational

activity. This distinction is important in that only human subject research requires IRB review and oversight. The Children's Wisconsin HRPP has developed guidance to help with this assessment. Additional information can be found on HHS's Office for Human Research Protections (OHRP) web pages.

- The responsibility for initial determination of whether an activity constitutes "research" rests with the individual who has primary responsibility for the activity. This individual should make this determination based on the definitions of "research" and "clinical investigation" as provided by the Common Rule and U.S. Food and Drug Administration (FDA) regulations, respectively (see section 5.1).
- Consultation with the Children's Wisconsin HRPP Office is encouraged.

Requesting a formal determination of whether an activity is human subject research

While a formal written determination of whether an activity is human subject research is not required, many investigators want this documentation to provide to publishers if requested. The Children's HRPP is the sole body designated to make formal written determinations at Children's Wisconsin.

- If ALL activity for the proposed project will occur at CW, this request can be made via Children's Wisconsin HSR Determination Form. The CW HRPP staff reviews and makes the determination, and the investigator will receive the form signed by HRPP staff indicating the determination.
- If some activity will occur at CW and some at Froedtert/MCW, this request should be made through the eBridge submission system. The reason for this is that in these cases both institutions need to make a determination about whether the activity occurring in their space is or is not human subject research. Both institutions use and have access to eBridge and can view the request.
- Any request for a formal written determination that an activity is research not involving human subjects must include materials in sufficient detail to make the determination.
    - Protocol or detailed description of the activity.
    - Consult with appropriate CW administrator(s) of the department(s) where the activity will be conducted to ensure there is institutional support for the activity.
    - A project being conducted by a resident/fellow/student (including nursing students) or an individual who is not faculty/staff at CW/MCW must also include with this request written departmental approval from an appropriate CW administrator to indicate project support.

  - For requests that involve obtaining de-identified or coded data or biologic specimens that are stored in a bank or registry, provide reference to the IRB-approved banking or registry protocol, or include the banking/registry protocol with sufficient operational details for evaluation.
- Investigators conducting research under the auspices of Children's Wisconsin **may not rely upon determinations made by other organizations** or through the use of electronic (or other) determination tools.
  - Children's Wisconsin will not make a not human subject research determination about activities conducted at another institution.
- For projects being conducted by any nursing students or being led by nurse personnel/investigators/scientists, please review the Children's Wisconsin Nursing Research web page
  - For Quality Improvement projects please consult with Holly O'Brien, Director Quality& Patient Safety, and provide written administrative acknowledgement with this request for determination.
  - For and Evidence Based Practice projects, please consult with Karen Gralton, PhD, RN, Evidence-Based Practice Specialist and provide written administrative acknowledgement with this request for determination.