Purpose of this manual

This manual is intended to provide investigators planning to do research at Children's Wisconsin with important information and guidelines about considerations when planning the research and steps to be taken prior to submitting your project for IRB approval.

This manual also covers guidelines and information related to the ongoing conduct of research at Children's Wisconsin. Investigators should also be familiar with and refer to Children's Wisconsin SOP manual which outlines federal regulatory, local, and institutional requirements to be followed when conducting research at Children's Wisconsin, as well as the Investigator Resources on the Children's Wisconsin HRPP pages, and Children's Wisconsin Connect Intranet Human Research Protection Program Channel.

This is the initial publication with more sections and content to be added in future updates

Full TOC

BACKGROUND – HUMAN SUBJECT RESEARCH					
Regulatory and Ethical Framework of Human Subject Research	IRBs of Record for CW and the CW HRPP				
PRE SUBMISSION and PRE APPROVAL					
Checklist – Preparing to conduct research at CW	Getting Help – consulting with the CW HRPP	Project Types	CW Engagement in research	Review Pathways Human Subject Research	Research Team Requirements
Feasibility assessment	Using Resources at CW	CW Data Storage and Security	Privacy and Confidentiality	Recruitment and Enrollment planning	Assent/Parental Permission/Consent Planning
HIPPA considerations	COI disclosure and management	Funding	Investigator Initiated Research	Sponsored Research	Special Populations – Considerations and Planning
Wisconsin State Laws that may Impact Research at CW	Scientific Review				
THE REVIEW PROCESS – Future Update					
Submitting Projects for Review/Review Flow	Regulatory Review Pathway				
POST APPROVAL – Future Update					
Modifications to Research	Reporting Non-compliance and Adverse Events and unanticipated problems	Continuing Reviews/Project renewal	Post approval Monitoring	Closing a study	

Table Of Contents

Part 2 - PRE SUBMISSION and PRE APPROVAL

3. **Checklist – Preparing to conduct research at CW**
4. **Getting Help – consulting with the CW HRPP**
   - Virtual Office Hours
   - Consultations
   - Contact information
5. **Project Types and Review Requirements**
   - Human Subject Research v. Not Human Subject Research
   - Multi-Site Human Subject Research and Reliance Agreements
   - Multi-Site Research s-IRB Review
   - FDA Regulated Research
     - IND
     - IDE
     - EFIC
   - Treatment Use (Expanded Access/Compassionate Use)
     - Drugs
     - Devices
     - HUDs (Humanitarian Use Devices)
6. **CW Engagement in research**
   - What does it mean for an institution to be "engaged" in research?
   - What will happen if CW is engaged in the research
   - How recruitment activities at CW may engage CW in the research
   - How recruitment for CW research at other institutions affect engagement
   - Request an engagement determination
7. **Regulatory/IRB Review pathways for Human Subjects Research**
   - Pediatric Risk Levels
   - Greater than Minimal Risk Research (convened board review)
   - Minimal Risk Research (Expedited review or Exempt determination)
   - Regulatory criteria for IRB approval
8. **Researcher and Research Team Requirements**
   - Who should be listed on the study team
     - Requirements and Qualifications
   - Who can be a Principal Investigator at Children's Wisconsin
   - PI responsibilities
   - Other investigators and key personnel
   - External Collaborators
   - Delegation of Responsibilities to the study team
   - Conflicts of interests and disclosures
9. **Using Resources at CW**
   - CW EPIC access
   - pTRU

- Imaging/Radiation
- Imaging MRI
- Request for CW Research Resources
- Departmental Sign off
- Department intake forms and processes

10. Recruitment and Enrollment planning

- General guidelines
- Initial contact guidelines
- Email recruitment
- Social Media
- Screening and waivers
- Recruitment for research at other institutions
- Data Warehouse and aggregate Tools

11. Assent/Parental Permission/Consent Planning

- When Parent is also a subject
- Plan for when 2 parent signature is needed
- Assent requirements and recommendations
- AOM plan
- Consent templates and change requests
- Working with sponsors on Consent language
- Special consent/parental permission considerations
    - Limited English Proficiency subjects
    - Blind
    - Limited literacy
    - Witnesses
    - When parent of the subject is a minor
    - Emancipated minors
    - Guardianship/LAR situations
- Remote consent
- Documenting the consent discussion
- Consent discussion checklist
- Electronic consent
- Waivers
- Templates

Future Updates Will Include:

- Feasibility assessment
- Wisconsin state laws that may impact human subject research at CW
- Conflict of interest disclosure and management
- HIPAA considerations
- Privacy and Confidentiality
- CW data storage and security
- Investigator initiated clinical trials
- Sponsored research
- Funding considerations
- Special populations – considerations and planning
- Scientific review
- Submitting project for review/review flow
- Regulatory review pathway
- Post Approval Topics
    - Modifications to human subject research projects
    - Reportable events – reporting non-compliance, adverse events, and unanticipated problems
    - Continuing review of research
    - Post approval monitoring
    - Closing a research project

1. Regulatory and Ethical Framework of Human Subject Research

The Belmont Report

"The U.S. has regulations to protect research subjects that are based on a core set of ethical principles. Three principles—**respect for persons, beneficence, and justice** were identified and explained in the 1979 Belmont Report. These Belmont Principles became the ethical foundation of the first comprehensive set of Federal regulations to protect human subjects in research, enacted shortly after the Belmont Report was published.

While the regulations have been updated since that time, their ethical foundation remains the same." (HHRP eLearning Program – Lesson 1)

- **Respect for Persons**

  Acknowledges that individuals make decisions about how they want to live their lives, including if they want to volunteer for research studies (informed consent).

- **Beneficence**

  Acknowledges that research could bring about important contributions to public good (minimizing risks).

- **Justice**

  Concerned with the fair distribution of burdens and benefits (equitable selection of subjects).

Federal Regulations

The primary Federal Regulations governing human subject research and the protection of human subjects are found in the US Code of Federal Regulations at 21 CFR 56 (FDA) and 45 CFR 46 (HHS). There are also federal regulations governing HIPAA.

Health and Human Services (HHS) Regulations – 45 CFR 46

The "Common Rule" (45 CFR 46) provides a broad set of protections for research subjects. These protections include review and approval of research protocols by IRBs and requirements for informed consent and privacy and confidentiality protection, among others. Regulations at 45 CFR Part 46, and its Subparts provide basic protections for people who participate in research that comes under HHS's purview.

The subparts establish additional protections for "vulnerable" subjects.

- **Sub Part A** – Basic HHS Policy for Protection of Human Research Subjects
- **Sub Part B** - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
- **Sub Part C** - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
- **Sub Part D** - Additional Protections for Children Involved as Subjects in Research

HHS-funded research must comply with both the Common Rule and the other subparts of the regulations. **Children's Wisconsin applies different but equivalent policies and procedures for some research not covered by regulations.**

The Common Rule (subpart A of the HHS regulations) was recently revised. These revisions became effective in 2018, but its compliance date was delayed until January 21, 2019. Nevertheless, the revised rule is officially called the "2018 Requirements," although many continue to refer to it as the "revised Common Rule," or simply the "new Rule."

For additional details about The Common Rule and its subparts see OHRP eLearning Program – Lesson 1.

FDA Regulations – 21 CFR 50

The FDA has its own regulations that apply to the clinical investigations it oversees. These regulations align with the Common Rule, but also differ in some important ways. While there is an ongoing effort to harmonize them, it is important for investigators and IRBs to know which regulations are applicable for a particular research project.

When research studies involving products regulated by FDA, the FDA regulations govern that research. If the involves FDA regulated products and is also funded/supported by HHS, the research institution must comply with both the HHS and FDA regulations.

Comparison of FDA and HHS Human Subject Protection Regulations

While HHS and the FDA are trying to harmonize these sets of regulations, there are differences that investigators need to be aware of when research is subject to both the Common Rule and FDA regulations. The FDA has a table comparing these 2 sets of regulations.

State Statutes

In addition to the federal regulations, there may be state specific statues that effect the conduct of research. Investigators should be familiar with any applicable state statutes.

Institutional Policy

Institutions implement their own institutional policies and procedures, which may be more protective than the regulatory requirements. Institutions may have a mechanism to enforce their own requirements, even though the Federal government may not have regulatory authority over research when it is not supported by a Common Rule agency.

Regardless of which IRB is serving as the IRB of record, investigators are expected to follow Children's Wisconsin HRPP SOPs when conducting research that engages Children's Wisconsin (eg. Research being done in CW space, use of CW resources to support the research, enrolls CW patients or involves access to CW medical records).

2. IRBs of Record for CW and the CW HRPP

IRB Services Agreement between MCW and CW

Children's Wisconsin and the Medical College of Wisconsin entered into a research agreement that went into effect July of 2022, which specifies that CW will rely on the IRB services of the MCW pediatric IRBs as our primary IRBs of record.

CW may also rely on other organization or independent IRBs to serve as the IRB of record for some projects as deemed appropriate by Children's Wisconsin HRPP leadership, such as when required by the Common Rule or NIH single IRB mandate (e.g. NCI IRB). In these cases, a request for a reliance/deferral on another IRB will be needed and this process is discussed later in this manual.

Consistent with the terms of the agreement, Children's Wisconsin maintains a Human Research Protection Program (HRPP), and its own FWA, to oversee research conducted in Children's Wisconsin space or with Children's Wisconsin data. In addition to IRB approval, Children's Wisconsin must also, as an institution, approve the research to be conducted at CW after conducting a review (local context review) to be sure that CW resources are available and able to support the research, that CW HRPP policies are followed, assess and manage any conflicts of interest, among other things discussed below.

What an IRB does

See article Institutional Review Board – What is It? For more details

Scope of authority of an IRB: 21 CFR 56.109 and 45 CFR 46.109.

An IRB's scope is limited to oversight of research involving human subjects. Research determined to be exempt, or to not involve human subjects does not require IRB review and oversight. The scope is also limited to making regulatory determinations about proposed human subject research. The scope if IRB of review focuses on determining whether a research project meets regulatory criteria of approval, and after approval, overseeing the study from a regulatory perspective until it closes.

What the CW HRPP does

See the article Human Research Protection Program – What Is It? for more details

The industry standard defines a Human Research Protection Program as "a shared responsibility for the welfare of subjects in research, involving multiple components, filling in the myriad gaps surrounding the jurisdiction of the IRB. With all such components interconnected properly, a "safety net" is formed to help ensure the optimal protection of the rights and welfare of the subjects."
Source: IRB Management and Function, Third Edition, Chapter 1-2

Scope of the CW HRPP:

Children's Wisconsin applies its HRPP review and oversight to all research regardless of funding source, type of research, or place of conduct of the research. The organization exercises these responsibilities through relationships with researchers and research staff, IRBs, sponsors,

participants, and the community. The CW HRPP is a part of the review of any research being conducted in CW space, with CW resources, or involving CW patients.

Institutional Policies and Local Context:

It is the expectation of the Children's Wisconsin HRPP that the IRB of record and investigators will follow Children's Wisconsin HRPP policies and local context requirements and practice, and will ensure consistency when making regulatory determinations as long as Children's Wisconsin HRPP policy does not conflict with applicable federal regulations.

3. Checklist – Preparing to conduct research at CW

There are a number of considerations and preparatory steps that must be taken **before** submitting an application for proposed research in the electronic submission system for CW HRPP and IRB approval. The submission of the application to the IRB of record should be the **final** step of preparing for a new research project to be conducted at Children's Wisconsin.

These pre-submission considerations will guide what information to provide in your application, indicate the appropriate review pathway, ensure that it is feasible for the research to be conducted, and this preparation will help avoid delays in the review after submission.

There is a Pre-submission checklist available to help investigators be sure all the appropriate considerations are addressed before submitting a project. If assistance is needed in working through these considerations, contact the CW HRPP office at CWHRPP@childrenswi.org.

4. Getting Help – consulting with the CW HRPP

When an investigator is in need of direction, guidance on projects being conducted in CW space, using CW resources or CW patients/data, the first contact should be the CW HRPP office. The CW HRPP will reach out to the MCW pediatric IRBs or other IRB of record as needed for additional information or to bring them into the discussion when appropriate.

Virtual Open Office Hours

Virtual Open Office Hours are on a first come, first served basis and are designed for study teams who seek help for general questions and guidance that may be provided quickly. To set up an appointment, please contact Kristin Costello at kcostello@childrenswi.org. Virtual Open Office Hours are held weekly, every Tue 9:30 – 11:30am via Zoom.

Consultations

Consultations are available to study teams and researchers who have complex questions or issues that may take significant time (>15-minutes, for example) to resolve. To schedule a consultation, please complete our consultation request form.

Contact Information

Questions should be directed to the general office phone or mailbox. Your questions will be directed to an appropriate staff member who will be happy to help you. The Children's HRPP/IRB always aims to reply as soon as possible, but due to the nature and volume of requests, please allow **three business days** for a response.

Children's HRPP Phone: (414) 337-7133 Fax: (414) 266-4925	General questions: cwhrpp@childrenswi.org
Children's Wisconsin HRPP Children's Corporate Center 999 North 92nd Street Milwaukee, WI 53226	Reliance agreements & deferral requests: cwreliance@childrenswi.org

Poject Types and Review Requirements

a. Human Subject Research v. Not 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 - both the definition of "research" AND the definition of "human subject" - must be submitted to an IRB of approval and continuing oversight.
At times it may be difficult to discern whether a proposed activity constitutes research or human subject research, quality improvement or an operational activity.

The Children's Wisconsin HRPP has developed guidance to help with this assessment.

Other resources

- CW SOP Manual – section 4
- HHS FAQs
- HHS decision Tree

b. IRB Reliance Agreements and Multi-Site Research

i. Overview

For details and information on requesting a reliance and this review process, please see

- Guidance Multi-site Projects and Investigator Responsibilities
- Guidance – Reliance Agreements

Note: the research affiliation agreement set up a master agreement between Children's Wisconsin and the Medical College of Wisconsin for the MCW pediatric IRB committees to be the primary IRBs of record for CW. As such, a specific request for MCW to be the IRB of record is not required. CW maintains a Human Research Protection Program (HRPP) which is separate and independent from the MCW HRPP. The CW HRPP also provides oversight of any institutional requirements and considerations which is separate from the regulatory requirements regarding IRB determinations (what the IRB of record determines and requires). For more details see Section 2.

However, MCW is not the only IRB that serves as the IRB of record for CW. CW has master agreements with the National Cancer Institutes Central Institutional Review Board (NCI CIRB) as well as the National Marrow Donation Program IRB. Additionally, when CW is participating in a multi-site project the IRB at another institution may be serving as the IRB of record for the project. There may also be situations in which CW, as the only site (not a multi-site project) chooses to rely on another IRB. The process to establish a reliance on these other IRBs is different and discussed below and in the Guidance – IRB Reliance Agreements.

ii. Multi-Site Projects

NIH uses the term "multi-site project" to describe a sub-set of cooperative non-exempt human research where the same research procedures (i.e., the "same protocol") are conducted at two or more U.S. research sites under the control of a participating local site investigator at each site.

A multi-site project typically involves a lead site (lead PI) that manages the administrative functions of the project in addition to conducting the same research procedures at the participating sites. A multi-site project could be a clinical trial, an observational study, or a basic clinical research study.

Children's is a separate location (institution) from Froedtert Hospital, Versiti, or MCW. A study would be considered a multi-site research project if Children's is included in a study also being conducted at Froedtert Hospital, Versiti, or MCW. See the Guidance Multi-site Projects and Investigator Responsibilities for details and the eBridge submission requirements.

Any institution that is engaged in human subjects research, is required by federal regulations to have an IRB/HRPP overseeing the research activities at that institution. This oversight may be provided by an institution's local IRB, the IRB at another institution, or a commercial IRB. Some projects (for example projects funded by the NIH) have a mandatory requirement to utilize a single IRB for all participating sites.

"When an institution relies on an external IRB that it does not operate, the institution and the IRB must document the institutions reliance on the IRB and the responsibilities that each entity will undertake as required by the Common Rule (45 CFR 46.103(e)" (IRB Management and function)

iii. Reliance Agreements and How to Request

Reliance agreements allow institutions to delegate IRB review responsibilities to an external IRB or a single IRB of record.

A reliance agreement (also known as an IRB Authorization Agreement, or IAA) is a formal contract between institutions that allows one IRB to act as the reviewing IRB for another institution or for multiple institutions involved in a research project.

- **Master agreements** are set up between an institution and an IRB to oversee a range of studies under a pre-established master agreement. Once established the institution and the IRB do not have to negotiate the terms each time the CW agrees to rely on that IRB for a study under the perview of that agreement. Examples of master agreements that CW has established include:
  - Research affiliation agreement with the Medical College of Wisconsin
  - Reliance on the NCI CIRB for studies with the Children's Oncology Group consortia
  - Reliance on the National Marrow Donation Program (NMDP) IRB for studies with this consortia
  - Use of the SMART IRB agreement to serve as the master agreement when relying on another site that utilizes that agreement

- **IRB Authorization Agreements** are agreements that are set up on a case by case basis between CW and the institution whose IRB will serve as the IRB of record. These are needed when there is not a master agreement already in place with that IRB, or the institution does not utilize the SMART IRB agreement.
  - This process is longer and more involved requiring negotiation of the terms of the agreement in involvement of CW legal department to set this up.
  - CW strongly prefers that the institution who will serve as the IRB of record utilize the SMART agreement to set up the reliance

Both types of agreements serve the same purpose of establishing the terms of an IRB to serve as the IRB of record for an institution to provide IRB review and make IRB determinations for a particular study. In all cases the IRB and the institution have their own responsibilities for the oversight of the research and protection of human subjects. Both the IRB of record and the institution have general responsibilities for the reliance (described in our guidance) but each agreement will describe the details of those responsibilities for a particular agreement and the research involved. However, the process for requesting, and setting these up are different and requires working with the CW HRPP.

The Guidance -IRB Reliance Agreements - provides more details regarding IRB reliances, including:

- Description of the SMART IRB agreement
- IRB responsibilities in reliance agreements
- Institution responsibilities in reliance agreements.
- Shared responsibilities of the IRB and the institution in reliance agreements
- The process of setting up a reliance agreement for research being done at CW
- Master agreements for consortia group research (Children's Oncology Group and National Marrow Donation Program)

c. FDA Regulated Research

Research is governed by Food and Drug Administration (FDA) regulations when the research involves a human subject and an FDA-regulated test article, or human subjects research data will be submitted to or held for inspection by the FDA. In these instances, the research must follow
both Department of Health and Human Services (DHHS) and FDA human subjects research regulations (Table comparing these provisions)

- IND
- IDE
- EFIC

d. Treatment Use (expanded access of investigational medical products) for Individual Patients

"Expanded Access - Sometimes called "compassionate use", expanded access is a potential pathway for a patient with a serious or immediately life-threatening disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available."

"Whenever possible, an investigational medical product should be used as part of a clinical trial. However, if patient enrollment is not possible (e.g., patient ineligibility, lack of ongoing clinical trials), or enrollment in a clinical trial is not feasible (e.g., distance to a trial precludes access), expanded access offers a possible route for gaining access to an investigational medical product."

The treatment with investigational drugs or devices is not considered a clinical investigation (research). As such, the institutional and review pathway, as well as the regulatory requirements, are different than for research studies being submitted for IRB/CW HRPP review and approval.

Approval to use an investigational product requires approval by:

- FDA
- CW HRPP when the treatment is occurring at CW
- MCW IRB/ IRB Chair (CWs primary IRB of record)

However, when there is no time to get prior CW HRPP or IRB approval, and the patient has an immediately life threatening condition, treatment can proceed AFTER FDA gives approval for **emergency use**, without waiting for IRB approval.

Investigators are STRONGLY requested to alert the CW HRPP of any possible treatment use **AS SOON AS YOU BECOME AWARE** this is a potential pathway. The CW HRPP will provide guidance as needed as well as work with the MCW IRB to make the review process as smooth and efficient as possible.

General information about Expanded Access/Treatment Use/Compassionate Use

- Expanded Access – Information for Physicians (including how to submit requests to the FDA)
- Expanded Access
- Expanded Access Categories for Drugs
- Expanded Access for Medical Devices

Treatment use of an investigational product requires a submission via eBridge for review by both CW (when the treatment is occurring at CW) and by the MCW IRB (CWs primary IRB of record).

- Children's Wisconsin guidance and submission checklist for single patient treatment use of investigational drugs
- Children's Wisconsin guidance and submission checklist for single patient treatment use of investigational devices

e. HUDs – Humanitarian Use Devices – Approval and Use at Children's Wisconsin

A Humanitarian Use Device is a medical device, which falls under FDA regulations, intended to benefit patients in treatment or diagnosis of a disease or condition that affects, or is manifested in, not more than 8,000 individuals per year in the United States. The incidence limit was raised from 4 to 8 thousand with the passage of the 21st Century Cures Act. (21 CFR 814.3(n))

"A HUD is a legally marketed device, and its use within its approved indication does not constitute a clinical investigation. However, IRB or appropriate local committee approval is required before a

HUD can be used at a facility for clinical care, with the exception of emergency use." (IRB Management and Function, Chapter 11-5)

While many uses of HUDs are treatment use HUDs can also be part of a clinical investigation – in these cases the submission and approval pathway is the same as any other human subject research activity.

When a HUD is being used to treat a patient at CW (not part of research), CW HRPP and IRB review and approval is still required. There are considerations and specific responsibilities when using a HUD:

- IRB responsibilities
- Physician Responsibilities
- CW specific requirements
- Reporting requirements

Details about HUD, additional references, considerations and CW requirements as well as how to submit for approval of this use can be found in the CW Article - "Humanitarian Use Devices (HUD) – Approval and Use at Children's Wisconsin."

5. CW Engagement in Research

What does it mean for an institution to be "engaged" in research?

Engagement in Human Subjects Research =

- the need for CW HRPP and IRB of record review and oversight of the activities occurring at CW;
- the activity occurring at the institution being subject to all applicable regulations, laws, policies, and requirements.

"In general, an institution is considered engaged in a particular non-exempt human subjects research project when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research."

What will happen if CW is engaged in the research

Knowing whether an institution is "engaged" in research highlights the obligations of an institution to regulatory and institutional requirements regarding the conduct of research, including IRB review and oversight of the research activities occurring at that institution.

Any research activities occurring at CW that engages CW must be reviewed, approved and overseen by an IRB. If CW is engaged and the IRB of record is not the MCW pediatric IRBs, a formal reliance agreement will need to be executed to defer IRB oversight of the research activities occurring at CW to that IRB. In the case of the Cooperative Groups we work with (Children's Oncology Group, National Marrow Donor Program) we have a standing master reliance agreement established with the IRB utilized by these groups (NCI CIRB and NMDP IRB).

Investigators cannot determine themselves whether an institution, including CW, is engaged in a research project. **Individual institutions make their own determinations regarding whether they consider themselves engaged in a research project**.

For more details see the article "Engagement in Research" which includes:

- How recruitment activities at CW may engage CW in the research
- How to request an engagement determination

Please consult with the CW HRPP office for assistance in determining whether plans to assist another site recruiting subjects for their research engages CW.

6. Regulatory/IRB Review Pathways for Human Subjects Research

Risk Levels of Pediatric Human Subject Research

Research involving human subjects follow one of several review pathways depending on the details of the project and the risk level. Pediatric Risk levels, defined in Subpart D of the Common Rule, differ from risk levels that apply to research involving adults in both definition and the practical effect on the conduct of research with children.

Research with children that involve more than minimal risk must be reviewed by the convened IRB – it does not meet the regulatory criteria for review by either exempt or expedited pathways.

"Minimal risk" means that 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. 21 CFR 56.102 (23) (i); 21 CFR 45.102(i).

IRB Review Pathways – Human Subject Research

When a study meets the criteria to be considered Human Subjects Research (HSR), the study will fall into 1 of 3 categories for review: Full Board, Expedited, or Exempt.

See article on the investigator resources page for full details on this topic.

Convened ("Full") Board Review: A "full board" review is one that takes place at a convened meeting at which a majority of members must be present, including a member whose primary concern is in a non-scientific area, before official actions may be taken. In order for the research application to be approved, it must receive approval of a majority of those members present at the meeting. Approval of the project requires it meeting the regulatory criteria for approval found at 45 CFR 46.111 and 21 CFR 56.111. If a project does not qualify for expedited review or an exempt determination, it must be reviewed via this pathway.

Expedited Review: An expedited review procedure consists of a review of research involving human subjects by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB in accordance with the requirements set forth in 45 CFR 46.110. An expedited review happens outside of a scheduled meeting and does not need to be reviewed by the entire committee. "Expedited" does not mean that a project is getting a faster, a prioritized, or an abbreviated review. To qualify for an exepedited review pathway, the research must meet regulatory criteria for one of the expedited categories (discussed below). Approval of the project requires it meeting the regulatory criteria for approval found at 45 CFR 46.111 and 21 CFR 56.111.

Exempt Research: Some research may be determined to be "exempt" - which means while it is human subject research, it is exempt from the regulations regarding human subject research, including being subject to IRB oversight once the determination is made. To qualify for an exempt determination, the research must meet regulatory criteria for one of the exempt categories (discussed below). The regulations do not specify who at an institution may determine that research is exempt under 45 CFR 46.101. However, OHRP recommends that, because of the potential for conflict of interest, investigators not be given the authority to make an independent determination that human subjects research is exempt. At Children's Wisconsin, we have delegated this determination to the IRB of record as described in section 5 of the CW HRRP SOP manual.

Greater than Minimal Risk Research

For pediatric research, when a study meets the criteria to be considered **Greater than Minimal Risk**, the study must be reviewed by the convened board, to which it is assigned, during a regularly scheduled meeting, prior to approval.

It is important to note that studies may have a combination of procedures/interventions that are Greater than Minimal Risk AND Minimal Risk. For example, a study may include administration of an investigational drug (which is a greater than minimal risk procedure) and medical record review (which is a minimal risk procedure). When this occurs, the study will still go to the convened board to make a determination.

Minimal Risk Research

Minimal Risk study reviews fall into 1 of 2 review categories: Expedited review or Exempt Review.

Expedited Review

When a study meets the one of the regulatory criteria for expedited review (one of which is that the project is considered solely Minimal Risk) the study can be reviewed by members of the IRB/HRPP without the need for convened board review. This means that rather than being reviewed by the entire committee at a regularly scheduled meeting, an IRB chair, or committee member delegated by the chair, can review the project outside of the scheduled meeting.

The expedited reviewer can approve a project or request modifications. However, they cannot disapprove the project. If an expedited reviewer feels the project may be approval the project will be reviewed by the convened board to make that determination.

Exempt Review

Some types of human subject research may be eligible for a determination that the project is exempt from the federal regulations for human subject research. This includes being exempt from IRB oversight. The institution, not the investigator, makes the formal determination of whether a project meets the exemption criteria. (45 CFR 46.104(d).

The purpose of these exemptions is to minimize IRB oversight that may be unnecessary for studies that pose minimal risk to subjects, and provide some benefit to the public. If an institution makes a determination that a human research project is exempt, then the federal regulations regarding human subject research do not apply to that project. However, this determinations does not exclude the project from institutional requirements (including HIPAA regulations) that may apply.

The Common Rule federal regulations include eight exemption categories. In order for a research project to be exempt it must meet the criteria of one of these exempt categories

Exemption categories not available for research being done at CW:

Category 2, which addresses interactions with subjects in the form of tests, surveys or interviews, has a limitation on being applicable to children. This category does not apply to children unless the research involves educational tests or observations of public behavior and the investigator does not participate in the activities being observed

CW does not utilize exemption **categories 7 and 8**. These categories related to limited IRB review for the storage, maintenance, and secondary use of identifiable private information or identifiable biospecimens using broad consent. Because CW does not allow broad consent, these categories of exemption would not apply to any studies being conducted at CW.

Approval Criteria for IRB Approval of Human Subjects Research

In order for the IRB to approve human subjects research through Full Board/Convened Board review or Expedited review, there are federal, regulatory criteria that must be satisfied for approval. The HHS and FDA federal regulations are aligned regarding the criteria for approval.

45 CFR 46.111 – HHS regulations
21 CFR 56.111 – FDA regulations

7. Researcher and Research Team Requirements

Who should be listed as study team members? – Key Study Personnel

Key Study Personnel (KSP) include the Principal Investigator, other investigators, and research personnel working on a human research study at Children's Wisconsin who are directly involved in conducting research with study participants or who are directly involved in using study participants' identifiable private information during the course of the research.

For studies funding by the National Institutes of Health (NIH) Senior/Key personnel is defined as "PD/PI(s) are always considered senior/key personnel and are always named in the Notice of Award (NoA). NIH program officials use discretion in identifying in the NoA senior/key personnel other than the PD/PI(s), and may identify individuals that are considered critical to the project, i.e., their absence from the project would have a significant impact on the approved scope of the project. The prior approval requirement for changes in status of personnel applies only to those senior/key personnel named in the NoA. Limiting the number of individuals that are named in the NoA does not diminish the scientific contribution to the project of the senior/key personnel not named in the NoA; it does reduce the number of individuals subject to the prior approval requirement." "The PD/PI(s) are always considered senior/key personnel. The PD/PI(s) should designate other personnel as senior/key only if they fit the definition (see above) or as instructed in the FOA."

Children's Wisconsin Training Requirements for study team members

CITI Training

All Key Study Personnel for research conducted at Children's Wisconsin must complete human subjects protection training on the Collaborative Institutional Training Initiative (CITI) website. The requirement to complete CITI training applies to all Human Subjects Research Key Study Personnel, including Exempt, Expedited and Full Board studies. IRB approval is contingent upon the fulfillment of this requirement.

Investigators and study personnel must be registered with CITI and affiliate with MCW (CW shares the account managed by MCW) on their CITI profile to select the modules. The CITI website has a Guide to Getting Started to assist with registering and accessing the courses.

The eBridge submission links to CITI and will indicate whether Human Subject Research training has been completed for an individual. However, please keep in mind that required training to conduct research at CW is an institutional, local context issue, and the Children's Wisconsin HRPP may have different or additional training required. Please consult the CW guidance on training requirements as well as the CW HRPP SOP Manual section 3 for up to date information regarding CW requirements. The training and qualifications of the study staff listed in the eBridge application is assessed and verified by the CW HRPP analyst during local context review.

PREP: Pediatric Research Education Program

In addition, CW has created the Pediatric Research Education Program (PREP). The Children's Wisconsin Pediatric Research Education Program is a multipronged initiative designed to support and empower clinical research staff through comprehensive training and professional development.

This program offers a robust variety of new staff education, continuous learning opportunities, novel research presentations, helpful reference materials, and individualized education upon request.

The goal of PREP is to foster a collaborative environment where clinical research staff can expand their knowledge, build connections, and stay in the forefront of pediatric research. Whether you are just beginning your journey or looking to deepen your expertise, this program is here to support you.

One of the educational offerings that is part of the CW Pediatric Research Education Program (PREP), is the the **CORe series.** The CORe series consists of 3 longer-form trainings: Children's Foundations, Operations, and Research Oversight. For the details, see the document PREP Overview and the FAQs document for more information on the requirements.

As an institution CW has designated completion of the CORe training series as **required** for all research staff who work in Children's spaces, Children's patients, and/or Childrens Wisconsin data.

The submission will not move forward to IRB review until all local training requirements are verified during the local context review by the CW HRPP office.

Who can be a Principal Investigator at Children's Wisconsin

The Principal Investigator is ultimately responsible for the oversight of conduct of the research at CW. While the PI may delegate certain study activities to other members of the study team, it is expected that the PI is assessing an individual's qualifications to carry out those activities and monitoring the study activities. The PI must provide active oversight of all study activities.

Per the FDA: "Investigators who conduct clinical investigations of drugs, including biological products, under 21 CFR Part 312, commit themselves to personally conduct or supervise the investigation. Investigators who conduct clinical investigations of medical devices, under 21 CFR Part 812, commit themselves to supervise all testing of the device involving human subjects. It is common practice for investigators to delegate certain study-related tasks to employees, colleagues, or other third parties (individuals or entities not under the direct supervision of the investigator). When tasks are delegated by an investigator, the investigator is responsible for providing adequate supervision of those to whom tasks are delegated. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study."

FDA Definition of Investigator:

From 21 CFR 312.3: Investigator means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. "Subinvestigator" includes any other individual member of that team.

From 21 CFR 50.3(d) and 21 CFR 56.102 and 21 CFR 812.3: Investigator means an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

HHS Definition of Investigator:

Per HHS: The HHS regulations at 45 CFR part 46 use the term "investigator" to refer to an individual performing various tasks related to the conduct of human subjects research activities, such as obtaining

informed consent from subjects, interacting with subjects, and communicating with the IRB. For the purposes of the HHS regulations, OHRP interprets an "investigator" to be any individual who is involved in conducting human subjects research studies. Such involvement would include:

- obtaining information about living individuals by intervening or interacting with them for research purposes;
- obtaining identifiable private information about living individuals for research purposes;
- obtaining the voluntary informed consent of individuals to be subjects in research; and
- studying, interpreting, or analyzing identifiable private information or data for research purposes.

PI at CW:

Any individual who plans to serve as the Principal Investigator for a research study at CW must meet the Children's Wisconsin requirements to serve as a PI. This will be assessed during CW local context review prior to a submission moving on to IRB review.

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.

As detailed in the policy *HRPP Conduct of Research on Human Subjects* - 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").

Students (Medical Students, Residents, Fellows, Nursing students, etc.) cannot serve as PIs. They are required to seek the sponsorship of an individual who meets the CW requirements who will serve as the PI on the study.

Children's Wisconsin does not recognize Co Principal Investigators – but other individuals can be listed on the study as investigators.

Any MCW faculty appointment, including adjunct faculty or Professor Emeritus, is a separate issue from whether an individual meets the CW requirements to serve as a PI on a study conducted at CW. This is an MCW designation and does not impact whether an individual meets the CW qualifications as a PI.

When human subjects research is being conducted at multiple institutions that include Children's Wisconsin, there **must** be a local PI to oversee any research activities carried out at Children's Wisconsin. This PI must meet the CW requirements to serve as the PI. More details can be found in the CW Connect article Multi-site Human Subject Research.

PI Responsibilities

The Principal Investigator (PI) of the study is the primary individual who ***assumes overall responsibility*** for the preparation, conduct, and oversight of the research study to ensure research integrity and safety, welfare, and rights of subjects. Furthermore, the PI is solely responsible for supervising all other study staff to whom study related responsibilities are delegated, and ensuring that all research activities are delegated to qualified individuals and performed in adherence with the IRB-approved protocol.

As the named PI of a research study, this individual must be qualified by virtue of education, training, and licensure/certification in the field that the study is being conducted in. The PI's responsibilities are an ongoing process, which begins prior to IRB submission of the study, carries through maintenance of the active study, and continues past study completion during the post-investigative phases.

Federal Requirements for PI Responsibility and Study Oversight

While the Common Rule itself does not outline specific investigator responsibilities, the Office of Human Research Protections (OHRP) addresses some Frequently Asked Questions on their website regarding their own interpretation of PI responsibilities, which can be found here. Most notably, OHRP states that "Investigators play a crucial role in protecting the rights and welfare of human subjects and are responsible for carrying out sound ethical research consistent with research plans approved by an IRB…[and] are responsible for ongoing requirements in the conduct of approved research."

Further, for studies that are FDA-regulated, the FDA regulations include specific PI responsibilities in 21 CFR 312.60-69 and 21 CFR 812 Subpart E. Most notably, the FDA requirements for investigator responsibilities include that the PI must:

- Ensure that the study is conducted according to the investigational plan and applicable regulations;
- Protect the rights, safety and welfare of subjects;
- Be responsible for all control of drugs and devices under investigation
- Be the primary individual responsible for adhering to the IRB-approved protocol
- Promptly report adverse events and unanticipated problems to the sponsor and the IRB

General PI Responsibilities

While certain responsibilities and tasks related to the study may be delegated to other authorized members of the study team (such as research assistants/coordinators, data managers, etc.), the PI is ultimately responsible for ensuring that the study is being conducted in accordance with the IRB-approved protocol. This extends to ensuring all study procedures are done in a safe and inclusive environment, and all aspects of the study maintain compliant with all applicable federal regulations and institutional policies.

As PI of a study, responsibilities begin prior to IRB submission. In the pre-planning phase of the study, the PI is responsible for:

- Ensuring that the protocol is scientifically sound, and compliant with all applicable federal regulations and institutional requirements.
- Chosen members of the study team are qualified by virtue of appropriate licensure/certifications to perform study related procedures

Throughout the study, the PI has various responsibilities related to maintaining study conduct and oversight, which may include, but are not limited to:

- Ensuring that the conduct of the study is compliant with the IRB-approved protocol at all times, to protect the safety, welfare, and rights of each research participant. This includes:
  - Oversight of the consent process to ensure that (1) informed consent is obtained for each participant prior to conducting study procedures, as required by the IRB and federal regulations, (2) informed consent is obtained by authorized personnel, and is documented appropriately, and (3) be present and available for any questions or concerns that might arise regarding study participation
  - Ensuring that no changes will be made to study procedures before being submitted and approved to the IRB via an amendment
- Ensuring that there are adequate resources to conduct the research, including:

    - Managing all research staff, including oversight of research staff training and education, ensuring that each individual to whom a task is delegated is appropriately qualified to perform each of their delegated tasks, assuring that all key personnel have met institutional training requirements (include link to institutional requirements) and have appropriate resources for conducting the study
    - Adhering to the study budget and adjusting it as necessary, and ensuring that all participants are appropriately compensated for study participation in a timely manner
- Ensuring that all aspects of the study are conducted in compliance with federal regulations and institutional policies, so as to protect the safety, welfare, and rights of each research participant
- Knowing which research regulations apply to their specific study, as well as any additional requirements that might be imposed by the study sponsor, institution(s) in which the study is being conducted, state specific laws, and/or funding agency
- Ensuring that all updates to the study, reportable events (including protocol deviations and unanticipated problems or events), and continuing reviews (if applicable) are submitted to the IRB in a timely fashion.
- Maintaining data confidentiality by frequently monitoring data storage and management processes
- Reviewing, preparing and submitting research results, as required by the sponsor
- Continuing communication with the study sponsor to stay up-to-date on all study updates that may be implemented via amendment, as well as communicating unanticipated problems and/or reportable events

Even when a study is completed, there are certain PI responsibilities that continue to carry over, including:

- Honoring confidentiality protections for any data collected, in accordance with the IRB-approved research plan
- Providing pertinent information about study results to research subjects, if applicable
- Honoring commitments to subject compensation for research participation

In addition to the general list of PI responsibilities outlined above, CW has specific requirements for all investigators conducting research at our institution, which can be found here.

PI Responsibilities for Handing Off a Study to a New PI

When a PI is planning to either step back from their role as PI or leave the institution, it is their responsibility to completely hand off the study to the next PI and ensure that they are aware of all PI responsibilities related to the study. A seamless handoff of PI responsibilities is imperative to ensure that there aren't any lapses in study progress or issues of noncompliance with the protocol.

In some instances, when a PI steps down from their role on the study, they may choose to stay on the study as a sub-investigator. When this is the case, the individual must either maintain their CW credentials, or have a plan in place to add their new institution as a relying site so that they may continue their involvement.

Other Investigators and key personnel at Children's Wisconsin

In order to serve as an investigator at CW, there are a number of requirements outlined in the policy *"Research: Conduct of Research on Human Subjects at Children's Hospital and Health System."*

In summary:

- If not a member of the CW medical/dental staff nor a CW or CHHS employee there must be an appropriate CW medical/dental staff member or CW/CHHS employee serving as PI as per the criteria outlined above and in this same policy
- ALL members listed as key personnel for a study MUST act within their scope of practice for their position and/or licensure
- An active medical appointment to the medical staff and clinical privileges to attend CW patients is required for key personnel to conduct clinical interventions or procedures as part of human subject research at CW.

External Collaborators

If an individual from another institution (including MCW and Versiti) will be serving as a consultant or collaborator decisions need to be made to determine how each investigator or individual will obtain appropriate IRB approval if needed.

The responsibilities of these collaborators and their activities at CW must be outlined in detail in the protocol or IRB submission to be able to evaluate whether their involvement may engage their institution (which would necessitate a reliance agreement), and whether they would meet our definition of key personnel, in which case we would need to assess whether they meet requirements defined in our policy.

Delegation of Responsibilities to the study team/key personnel

A principal investigator (PI) can delegate study-related tasks to their staff and colleagues, but they are still responsible for the tasks and their outcomes. The PI must ensure that the individuals they delegate tasks to are qualified by education, training, and experience (and state licensing or hospital certification where relevant) to perform the delegated task. Clinical interventions/procedures may not be delegated to any key personnel who does not have CW privileges/credentials to perform that activity. They must also have a plan for supervising and overseeing the activities delegated to any key personnel.

In order for an individual to be delegated study-related tasks, they must first be on the IRB-approved protocol. When a new individual is being added to the study staff via an amendment, it is imperative that they do not conduct any study-related procedures before IRB-approval is received. When an amendment is submitted to add additional study team members, the CW HRPP office and MCW IRB will both ensure that the staff member(s) being added have completed appropriate institutional training requirements, which can be found here.

Appropriate delegation is exceedingly important for tasks considered to be clinical or medical in nature, such as evaluating study subjects to assess clinical response to an investigational therapy (e.g., global assessment scales, vital signs) or providing medical care to subjects during the course of the study. However, all study procedures are ultimately the PI's responsibility. The PI is accountable for any regulatory violations that result from their failure to supervise the study adequately.

The investigator should maintain a list of all appropriately qualified persons to whom significant research-related duties have been delegated (a Delegation of Authority log). This list should also describe the delegated tasks, identify the training that individuals have received that qualifies them to perform delegated tasks (e.g., can refer to an individual's CV on file), and identify the dates of involvement in the study. An investigator should maintain separate lists for each study conducted by the investigator.

The PI must ensure that there is adequate training for all staff participating in the conduct of the study, including any new staff hired after the study has begun to meet unanticipated workload or to replace staff who have left. Children's Wisconsin has multiple resources to assist with education and training regarding human subjects research. PIs and key personnel are strongly encouraged to take advantage of these resources. Consult with the CW HRRP office and reference the Investigator Resources page.

When delegating study related activities, the investigator should have a plan to ensure that key personnel:

- Are familiar with the purpose of the study and the protocol;
- Have an adequate understanding of the specific details of the protocol;
- Are aware of all applicable regulatory requirements and accepted standards for the conduct of the study and the protection of human subjects;
- Are competent, experienced, certified and licensed to perform the delegated tasks;
- Are informed of any pertinent changes during the conduct of the study and receive additional training as appropriate.
- Are listed on the study team for the project approved by the IRB
- Are current with institutional training requirements
- Are familiar with CW Policies and SOPs

When the sponsor provides training for investigators in the conduct of the study, the investigator should ensure that staff receive the sponsor's training, or any relevant information (e.g., training materials) from that training that pertains to their role as a member of the study team.

Some examples of tasks that a PI can delegate include:

- Obtaining informed consent from study participants
- Preparing or dispensing investigational drugs or devices
- Conducting clinical exams
- Collecting vital signs or documenting medical history
- Assessing adverse events
- Assessing eligibility criteria
- Maintaining regulatory documents
- Completing Case Report Forms
- Coordinating scheduling of study related visits and procedure

Conflicts of interests and disclosures

It is CW policy to preserve public trust in the integrity and quality of research by reducing actual or perceived conflict of interest in the conduct of research.

The Principal Investigator is responsible for identifying whether any members of the study team have a potential conflict of interest to disclose, and if so, to make sure a separate disclosure form is submitted by each individual with the potential interest.

Pursuant to the Children's Wisconsin Corporate Compliance Conflict of Interest policy entitled *Research Conflict of Interest,* CW maintains a Research Conflict of Interest Committee (RCOI Committee). CW HRPP will collaborate with the COI Committee to ensure that COI of investigators and research team members

(investigators) are identified and managed before the IRB of record completes its review of any research application.

For CW HRPP purposes, investigator conflict of interest review occurs at the time of new study submission, continuing review, with the addition of a new investigator, and whenever an investigator updates their disclosure(s) indicating a new or changed interest. The disclosure is made by the investigator completing the *CW Conflict of Interest Supplemental Form* found on the CW HRPP website. When submitting a study in eBridge that engages Children's Wisconsin (CW), this supplemental form will capture whether you have a financial interest and/or personal relationship with a company, foundation, organization, etc. ("entity") that is associated with this research (e.g., sponsor, licensee, donor, provider of reagents/equipment/services, etc.) or with the technology to be studied.

The Research Compliance office notifies the Institutional official (IO)/Research Conflict of Interest Committee (RCOI Committee) whenever a submission is received which includes the supplemental form that indicates a possible COI. The RCOI committee reviews the investigators' disclosures and either notifies the HRPP staff that no investigator COI was identified or that one or more investigators has an interest that requires evaluation by the RCOI Committee. In the event a conflict that requires disclosure or management is identified, CW Research Compliance office will provide the HRPP a written summary describing the conflict and the conflict management plan (CMP). When the research is under an external IRB, any conflicts identified as the result of COI review and any CMP are provided to the external IRB in accordance with the IRB reliance agreement.

For more info on COI assessment and management refer to the CW HRPP manual, section 25. If you have questions about possible COIs and disclosures please contact the CW HRPP office.

8. Using Resources at CW

When any Children's Wisconsin resources will be used to conduct the proposed research (CW patients or their medical record, any CW clinical space – inpatient or outpatient, CW departments like the pTRU, any CW clinic, etc) this must be indicated on the application (or amendment form if applicable) in eBridge. This includes any study related activities being done at CW, including recruitment activities.

This will route the application to the CW HRPP office for local context review to ensure institutional requirements are met. This local review is required for any research being conducted at CW or using CW resources and is separate from the review of the IRB of record regarding the approvability of the protocol as written.

Children's Wisconsin EPIC Electronic Medical Record

CW utilizes Electronic Health Records for patient data vie EPIC. Epic's EHR software is used by hospitals, health systems, and other healthcare organizations to access, store, organize, and share patient records. Epic's EHR software includes features like medical templates, patient history, referrals, and reporting and analytics**.**

Researchers working in the Children's Wisconsin space must be granted access and have training on CWs EHR**.** To obtain access to the EHR contact CW Corporate Compliance.

For assistance with training and navigating the EPIC EHR contact Jeff Crawford at JCrawford@childrenswi.org.

How to request CW research resources to assist with your research at CW

There is an online form to request CW research resources for some Children's Wisconsin departments that have their own intake forms and require some specific information to assess their ability to support a research project. This should be completed for any of the applicable services requested, and the approval documentation included with the project submission in the electronic submission system.

Pediatric Translation Research Unit (pTRU)

The pTRU at Children's Wisconsin, located on the 2nd floor of the center tower of Children's Milwaukee Campus, offers a variety of services to assist researchers in carrying out their projects.

The pTRU offers space for research related visits for subjects with examination rooms and nursing support. All RNs are PALS certified nurses. They can assist with IV starts, investigational drug administration and phlebotomy services. They are able to draw clinical labs at the time of the research draw. They can also perform 12 lead EKGs when needed for a study (they do not provide reading and interpretation of these EKGs).

In addition to clinical services pTRU can provide a variety of other support for both funded and unfunded research. The pTRU has an EPIC Credentialed Research Trainer to assist with training and navigation of the EPIC EMR at CW. They can also provide assistance with FDA regulation and monitoring support for IND/IDE studies and budget consultation.

Lab services include: simple lab spinning, storing, and shipping of specimens. They can provide peripheral blood mononuclear cell (PBMC) preps for an additional processing charge. pTRU staff are IATA/DOT trained and have experience with serum, plasma, buffy coats, and Vortex mixing. Their lab has Biosafety Level (BSL) 2 designation and has equipment for sample storage such as: -80 freezer, -20 freezer, and refrigerator. They have a Baker Hood for safety when processing specimens, sterile alliquoting, dry ice for shipping, and they are a Genomic Science and Precision Medicine (GSPMC) DNA lab pick up site.

To inquire about pTRU assistance for your project, complete the pTRU intake form and pTRU staff will work with the investigator to assess whether they can adequately provide the requested services and any associated fee.

Imaging Services at Children's Wisconsin

When a project requires imaging service by the CW imaging department (including access to and de-identification of CW imaging records), this will require review by and coordination with the CW imaging department. Please see the Guidance document for full details. The use of radiation/imaging in a research project being conducted at Children's Wisconsin, and/or use of CW imaging records, needs to be reviewed as part of local context. The review will assess the logistics of the proposed use of CW imaging services and/or records (can the imaging department support the research project) as well as the need for radiation safety review–both locally and by the state of Wisconsin Department of Health and Human Services.

The CW imaging manager is the gatekeeper/point person at CW for all studies that will utilize imaging services at Children's. When a researcher needs to invoke use of any CW imaging services for their research, they must complete an imaging intake form to describe the details for review by the imaging manager who will assist with coordinating any safety committee reviews as needed.

This should be done **prior to** submitting the project in the electronic submission system, and any approvals (Imaging department, CW local radiation or MRI safety committee, and WI state approval if required) must be included with initial submission of the study in eBridge.

Any modifications to the research that add, or require additional imaging services, will need to undergo this same review process by imaging prior to submitting the amendment.

NOTE: some projects may use imaging services at both MCW/Froedtert Hospital and Children's Wisconsin. As an example, administration of radiation therapy on pediatric patients occurs at Froedtert, and there are some specific MRI scanners located in MCW/FH space. Each institution has their own process for reviewing this use and getting the required safety committee or state approvals. Described is the process at CW, but once use of CW imaging services is approved and verified during CW HRPP local context review, there may still be a pending or ongoing ancillary review by the MCW radiation safety office.

Because of how the routing works in eBridge, any project that indication use of imaging or radiation will be routed to the MCW radiation safety office as well as to the CW HRPP office. The CW HRPP office coordinates with MCW to mitigate unnecessary delays and moves on without MCW radiation safety review if this is not required when all imaging is being done at CW with CW equipment.

As always, please reach out to the CW HRPP office for any questions or assistance with this process.

Departmental Sign-off

What is departmental sign off?

Departmental sign-off provides a written agreement between the administrators of a department at CW and the study team, which allows the study team to conduct parts or all of their study in that department's space. It is important that departmental administrators give their permission and are aware of all research activities happening in their space.

Why do we need departmental sign-off?

The CW HRPP office has a local context requirement that research involving human subjects have departmental administrative review (department, laboratory, unit or clinic) when any procedures, tests, medications and/or space are to be provided by Children's as part of the research activities. The purpose of this review, and further the purpose of obtaining departmental sign-off, is to ensure that the administrators and involved departments are aware of the impact that the proposed research study may have on the area for which they hold administrative responsibility.

Examples include, but are not limited to:

- Nursing support (administration of study drug, additional assessments for study data capture, collection of blood/tissue samples to be performed by unit staff, etc.)
- Diagnostic testing (Radiology, Pulmonary, etc.)
- Laboratory processing/services (phlebotomy, sample processing, specific lab tests, etc.)
- Pharmacy (study drug storage, dispensing, etc.)
- Procedure specific support (ex: anesthesiology during a procedure)
- Recruiting
- Consenting
- Pediatric Translational Research Unit support (Nursing support, BodPod access, etc.)
- Survey/Questionnaire completion
- Blood samples and buccal swabs collected by your study's own staff

How to obtain departmental sign-off

For any departments that do not currently utilize the CW Research Resources Request Form, Departmental sign-off is obtained by using this attestation form, which should be included in the package submitted to the IRB. During our Local Context Review, the CW HRPP will look for departmental sign-off to be attached in Section 52 of the PRO application. Departmental sign-off must be included for ALL departments in which a research study is conducted.

The individual that should be giving approval via the attestation form should be the ***Children's Wisconsin administrator***, who provides leadership over the specific Children's area where the proposed study activities will take place. Support from the Medical College of Wisconsin faculty or staff, such as the provider serving as department chair, medical director, etc. is important, but not sufficient for this purpose.

Further, it is the PI and study team's responsibility to know who the appropriate Children's administrator is, as the CW HRPP office does not have this information readily available.

When providing departmental sign-off approval, the CW administrator signing the form is indicating the following:

- Awareness that study activities will take place in the children's area
- Awareness and agreement that patients in this area are being approached to participate in research
- Confidence that the research activity won't disrupt daily operations in a negative way
- Agreement that their area can support the research activity; that staff resources in the area are adequate and may be used for study activities as described in the protocol

9. Recruitment and Enrollment planning

Recruitment is generally the first contact between researchers and prospective participants (whether through paper-based or online announcements, media communications, or face-to-face interactions) and is a prelude to the informed consent process.

Numerous methods to recruit potential research participants exist; however, all methods involve presenting potential subjects information about the study to establish a subject's interest and willingness to participate in research.

When submitting a new research study, the PI should identify and describe in sufficient detail in the summary/application all methods of recruitment they will use to recruit and/or identify potential research subjects. The process and methods should be described from the first encounter with the subject/their data all the way through to the consent process and include (by role) which research team members will be involved.

Children's Wisconsin has specific, detailed guidance regarding recruitment at CW which should be consulted and followed when recruiting at CW. **All recruitment methods and materials used to recruit potential research subjects at CW must be reviewed and approved by the CW HRPP and the IRB of record prior to utilization.**

Recruitment Methods

Initial Contact Guidelines

When researchers are planning to enroll human subjects into a research study, there are many methods and approaches that may be taken for recruiting such participants. Across the board, the primary goal of recruitment involves presenting potential subjects with pertinent information about the study to establish a subject's interest and willingness to participate in research. Per the Federal Regulations, recruitment is considered part of the informed consent process; thus, it is expected that this initial contact and recruitment, in any form, is done ethically and respectfully, that the information presented is clear and accurately represents the research and what the participant can expect so that a decision to continue on with the research consent process and possible enrollment is informed and voluntary.

For more information about general recruitment guidelines, please see the CW Human Subject Recruitment Guidance document.

Record Review

Potential subjects may be identified by investigators/key personnel using medical records, clinical databases or research databases. This process is often identified as a "record review" or "screening" and requires IRB and Privacy Board approval, and appropriate consent and HIPAA waivers granted, prior to accessing patient records.

To conduct record review for recruitment purposes, it is important that the PI include the following information in the protocol summary/application:

- Do the investigators/key personnel have a treating relationship with potential subjects?
- Which members of the research team have been delegated to review the records?
- What identifying information will be collected/viewed to assist with the recruitment process?

The IRB may approve research in which the investigator will obtain information or biospecimens for the purposes of screening, recruiting or determining the eligibility of prospective subjects without

first obtaining informed consent if either of the following conditions are met: (1) The information will be obtained through oral or written communication with the prospective subject, OR (2) by accessing records or stored biospecimens.

As CW is considered a covered entity and must abide by the federal regulations regarding HIPAA, investigators should indicate in their protocol summary/application if they wish to screen or recruit subjects through record review, as a partial HIPAA waiver may be required.

In-person (face-to-face) Contact (avoiding "Cold Approaching")
Potential subjects who have been identified as possibly qualifying for a research project without their knowledge (via an IRB-approved partial HIPAA waiver for screening) must be initially contacted by an individual with a treating relationship to the potential subject (rather than an unknown member of the research team). This provides prospective participants with the opportunity to participate in the research study while simultaneously respecting their autonomy and protecting their privacy and confidentiality.

In addition, PIs who wish to approach and recruit CW inpatients for their research studies must also obtain the permission form the attending provider. This permission must be documented in the regulatory file, and this plan must be described in sufficient detail in the protocol summary/application.

Recruitment Letters, Emails, or Phone Calls (avoiding "Cold Approaching")
Recruitment letters/emails/phone calls are seen as a first step of the informed consent process and the subject selection process, and should contain the information as outlined in the Human Subject Recruitment Guidance document.

It is important to note that CW does not allow "cold contact" of potential subjects. In order to respect a patient's autonomy and privacy, it may be necessary for the PI to enlist the cooperation of other professionals and organizations as intermediaries in contacting a potential subject and obtaining permission from the subject/family to release their contact information to the investigators/key personnel. This permission should also include subject/family preference regarding how they will be contacted (letter, email or phone).

Some important things to remember when creating a plan for recruitment letters, emails or phone calls include:

- All email contact needs to be encrypted and subjects must be able to respond in an encrypted fashion.
- Approach letters should be printed on either departmental or project-based letter head and must be approved by the treating physician (who may also be the PI), and must describe how the subject was identified.
- When obtaining names through a public list, the PI should include the name of the public source in the initial communication.

Please note that investigators may not use MyChart (via EPIC) to communicate with potential subjects as a recruitment tool for research. If there are any questions about the use of MyChart for communication with subjects for research purposes, investigators may reach out to CW Corporate Compliance department.

For more details surrounding use of recruitment letters, emails, or phone calls, please refer to the Human Subject Recruitment Guidance document.

Use of Advertisements in Research

Advertising for or soliciting subjects is considered to be the start of the informed consent process and subject selection process.

When advertisements are used as part of subject recruitment processes, they must be submitted and reviewed prospectively by the IRB, and must be included with the PRO submission (or AME, if it is being added later as a recruitment method). The IRB will review the information contained in the advertisement and the mode of its communication to ensure that it is not coercive, unduly influential, and does not state or imply a certainty of cure or favorable outcome or other benefits beyond what is outlined in the informed consent document and the protocol. This is especially critical when a research study may involve subjects who are likely to be vulnerable to undue influence, such as children.

Additionally, approval from Children's Marketing and Communication Department must be obtained for use of the Children's logo. After an advertisement or press release has been approved by an IRB, it must also be submitted to the MCW Public Affairs Office for review and approval if the MCW logo will be included.

Some proposals for Human Subjects Research at Children's Wisconsin incorporate plans to post or distribute flyers or offer patient brochures/information to inform potential subjects about a particular research study. Children's Wisconsin has a family facing signage policy that outlines guidelines for all signage throughout the hospital. While adherence to this policy is generally required, exceptions may be made for research project participant signage due to its unique nature. For more information please see the CW HRRP Guidance on use signage at CW.

When preparing an advertisement, website or social media posting or recruitment letter to be used to recruit potential subjects to their research study, the PI should ensure the content of the advertisement is consistent with what is outlined in the Human Subject Recruitment Guidance document.

For a list of examples of acceptable advertisements, please refer to the Human Subject Recruitment Guidance document.

Scripts

For some research studies the first contact prospective subjects make may be with an individual who follows a script to determine basic eligibility for the specific research study. The CW HRPP and IRB must review the procedures and script/list of talking points to assure that they adequately protect the rights and welfare of the prospective subjects.

Internet or Social Media Recruitment

Use of social media platforms, such as Facebook, Instagram, and Twitter, to advertise research studies allows for broad reach and efficiency in recruiting participants.

If a local PI chooses to post direct recruitment advertisements or material via the internet or social media, IRB review and approval of the method and content is required. It is important to note that

this method of recruitment cannot be used to gather identifiable information from potential subjects. Additionally, if an investigator chooses to use social media as a recruitment method, the PI must describe in the protocol summary/application where and what listing(s) specifically are being used.

For more information about social media recruitment, please refer to the Human Subject Recruitment Guidance document.

Sponsor Recruitment Campaigns
When the overall recruitment campaign and other tools (such as radio and phone screening scripts) are not under the direct control of the local site and are intended to recruit potential subjects at a national level, the local IRB is not responsible for review and approval of these sponsor-specific recruitment methods and materials, since the persons viewing the campaign would not yet be considered Children's subjects.

If this method is being utilized at CW, it should be described in detail in the protocol summary/submission for the research study. Further, it is the IRB's expectation that when this method of recruitment is proposed, the sponsor has obtained appropriate approval from the IRB of record for the content of these recruitment materials and methods to be used.

For more information about social media recruitment, please refer to the Human Subject Recruitment Guidance document.

Data Warehouse and Aggregate Tools for Data collection

Children's Wisconsin has a number of "source systems" or data sources that can be utilized for research projects. For full details refer to this power point presentation. (This is available on the Connect Intranet. See section 3 of this manual for instructions on accessing Connect, or contact the CW HRPP to request this powerpoint)

- Data can be pulled directly from the source systems
  - Reporting Workbench and Slicer Dicer (EPIC reporting tools)
- Data analysts can pull data from source systems and combine that data into custom data reports
- Data from sources systems can be transferred into our Enterprise Data Warehouse (EDW)

iNSIGHT is a portal where custom reporting and applications can be viewed and run as needed.

- Custom reports based on specific criteria
- Applications built for specific customer groups that allow for filtering data, understanding trends, volumes, etc.

Access to **iNSIGHT** requires a few steps

- CHW employees and providers (MD,APN, NP, Fellows) have access to the Report Center and the applications (after the appropriate education)
- MCW employees can receive access after requesting access from CW Health Information Management department (on Connect the request form can be found under Service Agreements>Information Services) and completing the iNSIGHT basic elearning.

EPIC – The electronic medical record system for Children's Hospital has a number of tools available

- Analytics catalog – searching analytics content within EPIC

- SlicerDicer – allows user to pull customized data populations (this is not real time data) to explore a patient population and assist with prep to research
    - This tool uses models to find the appropriate population such as "visits", "EDTC Encounters", "Bedded Patients" etc.

For additional assistance in gaining access and learning to utilize these tools, please contact the pTRU for individualized help.

10. Assent/Parental Permission/Consent Planning

Consent templates and change requests

When creating consent documents for a project, consent templates should be utilized. These templates include language required by Children's Wisconsin. If MCW is serving as the IRB of Record, the MCW consent templates must be used.

- If the project is investigator initiated research, the investigator must complete the template with specifics of the project
- If the project is sponsored research and the sponsor provides model consents, this information must be transferred to the consent templates (this includes research sponsored by a consortia such as the Children's Oncology Group – COG).
    - There are special requirements for consent documents when the study is conducted by COG. Contact the CW HRPP office for assistance.
- If the project is multi-site research and the lead site provides a model consent, this information must be transferred to the consent templates.

If another IRB (not MCW) will be serving as the IRB of record, the templates provided for that IRB should be used and customized with local CW required language. This will be verified as part of the reliance process. Contact the CW HRPP for assistance as needed.

The MCW consent templates contain:

- **Blue language** – this language can be modified/added to in order to fully describe the specifics of a particular project. This can be modified without prior approval, but it will be reviewed by the CW HRPP and the MCW IRB and changes may be required
- **Black language** – This is template language. Some sections are specific to CW and the instructions will indicate this – if the project is being conducted at CW the CW template language must be used. This language **CANNOT** be changed without prior approval from CW HRPP and MCW. To request a change to the template language, a Change Request form must be submitted (scroll to the bottom of the page for the link to this document). If approved, the change request form should be included with the submission to indicate prior approval to any changes to black template language.
    - Sponsors often request changes to templated language. These changes may or may not be approved by CW HRPP or MCW. There must be regulatory justification for changes to the template language. If needed, the CW HRPP can meet with sponsors to discuss changes.

Assent of Minors to Participate in Research

Research that involves children – defined in Wisconsin as individuals under the age of 18 – requires consideration of obtaining and documenting the assent of children to participate in the research.

Please see the CW HRPP Guidance on assent with details regarding assent and the expectations at CW.

What the investigator needs to keep in mind:

- Assent is a minor's **affirmative** agreement to participate in the research. A child simply not objecting to participation in the research does not equal assent.
- Like consent and parental permission, assent is an ongoing process that should be re-confirmed throughout a child's participation

- The regulations are not proscriptive, but rather assign responsibility to the IRB of record to assess and determine whether assent should be required, what the process should look like, and whether documentation is required.
- There is no set age, in regulations or local CW policy, regarding the minimum age at which assent should be sought.
    - This judgment may be made for all children to be involved in the research under a particular protocol, or for an individual child, as the IRB deems appropriate.
- It is the IRB which has regulatory authority to determine that assent is **not** required for a particular study
- This inherent flexibility provides opportunity for researchers to propose an assent process in line with the CW HRPP perspective and the opportunity to inform the IRB of record about the rationale for a proposed assent process to aid the IRB in making their determinations.
    - The CW HRPP strongly encourages flexibility and creativity in using age appropriate and engaging mediums to help the child understand what their participation means – focusing on things that would be most important to the child in making a decision about their participation (what will I have to do, will it hurt, how long will it take.)
- Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with §46.116 of Subpart A.
- When the IRB determines that assent is required, it shall also determine **whether** and **how** assent must be documented
- The PI should describe their proposal for the assent process to assist the CW HRPP and the IRB of record in making a judgment regarding assent
- If an investigator feels a subset of potential subjects would not be capable and is requesting a waiver for that group, there should be an explanation of why that subset may not be capable and how this will be assessed (for example a documented diagnosis in the medical record that would render them incapable, specific tools used to assess and document a patient's capability)
- The regulations, nor the CW SOPs do not define how the assent of a child participant should be documented, or on what type of form. There is no regulatory or CW requirement defining what age ranges should sign a separate assent form v. the parental permission form, or that a child's signature is even necessary. It is perfectly acceptable to have all children sign a separate assent form. It is also acceptable for all children to sign the parental permission form as long as ALL children are presented with age-appropriate information in the assent discussion to aid their understanding of what their participation means so they can decide whether they are willing to participate.
- Dissent from the child overrides permission from a parent when the IRB has required assent
- Similarly, a child typically cannot decide to be in research over the objections of a parent.

The regulations have given the authority of the IRB to decide whether assent is required, whether documentation of assent is required, and whether the proposed process or requested waivers are appropriate. However, the regulations do not specify any particulars in terms of what is required regarding assent and the assent process, materials used to help the child understand, etc.

This means that the rationale provided by the investigator in the context of the specifics of the protocol, as well as the local context preferences of CW are important considerations for the IRB in making their determination about assent. During local context review the CW HRPP will assess the assent plan from an institutional perspective and may offer suggestions or request modifications to bring the plan in line with local context expectations.

The investigator should describe the assent process and any rationale for not obtaining assent and the age at which they feel assent is appropriate, whether and where they will have the child document their assent and

provide all related materials. The IRB will then determine whether they feel this is appropriate during review of the proposal.

Consent for Parents Who Are Also Subjects of the Research

In studies where parents are also subjects of the research (meaning, parents are actively being enrolled into the study and participating in research activities that involve collecting and/or analyzing data and/or biospecimens about themselves, as opposed to just providing information solely pertaining to their child), informed consent must be obtained from parents as adult subjects of the research.

In instances where parents are participating in the research study only by virtue of providing information about their child (who is a subject of the research), parents may not be considered subjects of the research and therefore informed consent does not need to be obtained from parents.

Consent where IRB requires 2 Parent Signatures for Subject Consent

The IRB of record must determine that adequate provisions have been made for soliciting the permission of each child's parent or guardian. Further, the IRB of record may find that the permission of one parent is sufficient for research to be conducted under Categories 1 (45 CFR 46.404/21 CFR 50.51) & 2 (45 CFR 46.405/21 CFR 50.52).

When a study falls under Categories 3 (45 CFR 46.406/21 CFR 50.53) & 4 (45 CFR 46.407/21 CFR 50.54), the IRB of record may find that permission from both parents is required for research to be conducted unless a) one parent is deceased, unknown, incompetent, or not reasonably available; or b) only one parent has legal responsibility for the care and custody of the child.

Permission from parents or legal guardians must be documented in accordance with and to the extent required by Section 14.7 of the CW HRPP SOP document.

Consent at Age of Majority

When a minor reaches the age of majority (the subject is now an adult - 18 years old in Wisconsin), if any research activities will continue for that subject, you will no longer have legally effective parental permission (considered the equivalent of informed consent in the case of a minor) or a valid HIPAA authorization. As such, consent will need to be obtained from subjects when they reach the age of majority.

There is a possibility that previously enrolled subjects will reach the age of majority after study closure, but during the 10-year records retention period during which time identifiable data may be stored. The assumption is that there would be no access of the stored data in the future, prior to destruction at the end of the retention period. In this case, consent and HIPAA waivers the age of majority would not be needed. However, if the PI anticipate the need to access or use the identifiable data after study closure, then the study would need to be reopened (and overseen by an IRB) and consent and HIPAA authorization, or waivers if appropriate, would then be needed for any subjects who have reached the age of majority.

For any research study that has oversight by an IRB, the PI must describe in the submission the plan to address consent and HIPAA authorization for any minor subjects who may turn 18 while still considered a human subject. The default expectation is to obtain and document consent and HIPAA authorization from the now adult subject when possible. However, a waiver of informed consent and HIPAA authorization at the age of majority will be considered in those cases where a subject's continued participation constitutes no more than minimal risk and meets the other requirements for waiver under 45 CFRF 46.116(d), including the requirement that the "research could not practicably be carried out without the waiver."

For more information on how to address an age of majority plan, and when a waiver at the age of majority is appropriate, please reference the CW HRPP Consent at Age of Majority Guidance document.

Special Considerations for Obtaining Consent/Assent/Parental Permission from Special Populations, and Use of a Witness

In some instances, investigators may be recruiting from special populations for their research studies. This may include, but is not limited to, consent of blind subjects and consent of subjects with limited literacy, the investigators must clearly outline in the consent plan how they will utilize witnesses to obtain consent from these populations.

Obtaining Informed Consent from Limited English Proficiency (LEP) Subjects

A subject with limited English proficiency is one unable, or with limited ability, to verbally comprehend the spoken English language or read and comprehend documents written in English. For individuals who speak languages other than English, or who possess limited English proficiency (LEP), informed consent may require an interpreter and a translated consent form.

Per Children's Wisconsin policy, Federal regulations, guidance from OHRP, and the FDA, there are two acceptable methods by which to obtain and document a subject's informed consent to participate in a research study when they are considered an LEP subject.

Preferred Method	Short Form Method
The Preferred Method is to provide consent forms written in a language understandable to the subject or the subjects legally authorized representative. When utilizing the Preferred Method for consenting LEP subjects/families, it is important to note the following: • The IRB of record must first approve all other aspects of the study (aside from translated material) with no further modifications required. The translations should be based on currently IRB-approved assent/parental permission/consent documents. These translated documents should then be submitted as an **amendment**. This prevents having to re-translate documents if there are modifications required to the English versions. ○ Translated documents MUST be kept up to date as there are modifications to the study and any of the study documents • CW HRPP requires that a certificate of translation be included with the submission of translated documents. CW HRPP does not require the use of a particular translation service to translate documents. • CW does NOT require back translations of any translated documents.	The Short Form Method should only be used for the occasional and unexpected enrollment of a non-English speaking subject when no prospectively IRB-approved translated consent documents in the appropriate language are available. The investigator may use oral translation of an IRB approved study summary to explain the study to obtain consent, and an IRB-approved "short form" to document consent (if one is available in the appropriate language). When utilizing the Short Form Method for consenting LEP subjects/families, it is important to note the following: • CW HRPP allows use of the short form **one time** per language in a study for an LEP subject. After that, it is no longer unexpected that subjects who speak a particular language may be enrolled, and for future enrollments in that language it is expected that fully translated documents will be used. • There are a number of short form consent templates available, which can be accessed here. Of note, at CW it is allowable to use the current IRB-approved parental permission/consent document as the summary for use in the consent discussion. • When a potential LEP subject is identified, the investigator should submit an amendment requesting use of the short form for a particular subject. Typically, this should be requested via an

• Subjects/parents should sign the fully translated assent/parental permission/consent documents and should be provided with a copy for their reference • An interpreter should be used for the discussion, even when there are translated documents, to assist with getting the potential subject/family questions answered. For more information about interpreter services, please see the CW Language Services page.	amendment immediately **after** there is an unexpected, identified subject for which no fully translated consent documents are available at the time of enrollment. • Per regulations, there must be a witness, who is fluent in both English and the subject's language, to the consent discussion done through an interpreter. The witness must be present for the entire discussion, not just the signature. Per OHRP, the interpreter may serve as the witness. • Consent is documented with signature on IRB-approved informed consent documents. A copy of the signed summary and short form is given to the subject or subject's legally authorized representative. ○ **Subject** (or their legally authorized representative) signs the short form. ○ **Person obtaining informed consent** signs the IRB-approved English consent document (summary). ○ **Witness** signs both the short form and the IRB-approved English consent document (summary).

Additional Special Circumstances

There are some circumstances when enrolling children in human subject research which require consultation with the CW HRPP. If needed, the CW HRPP with consult with Children's Wisconsin Legal Department. These include:

- Obtaining Assent/Consent/Parental Permission when the parent of a potential subject is a minor
- Obtaining Consent/Parental Permission from emancipated minors
- Obtaining Consent/Parental Permission for a child subject under guardianship and/or with a legally authorized representative

Remote Informed Consent

In situations where there cannot be face-to-face interaction with subjects, CW HRPP allows for the consent process to be conducted remotely. Informed consent must include a discussion of required elements as detailed above, and in most cases, is not valid consent until the subject has signed and dated the consent. For details regarding specific requirements for requesting approval of a remote consent process, please refer to Section 14.6.2 of the CW HRPP SOP document.

Electronic Informed Consent

The ethical obligation to obtain informed consent for participation in research is fundamental; however, U.S. regulations do not specify a particular method for the informed consent process. Recognizing the increased interest in using electronic informed consent (eIC) to replace or supplement the traditional paper-based process, OHRP and FDA issued a joint guidance on the topic in 2016.

Investigators who propose to use eIC should submit copies of all forms and informational materials (e.g., video content, hyperlinked webpages) that the potential subject will review during the eIC process. For more details about obtaining electronic informed consent, please refer to Section 14.6.2 of the CW HRPP SOP manual.

Requesting a Waiver or Alteration of Informed Consent

In certain cases, HHS federal regulations allow the IRB to waive some or all of the required elements to obtain informed consent or parental permission. This mainly applies to research that is no more than minimal risk, and is primarily requested for projects that involve secondary analysis of data (i.e., record review that does not involve direct contact with subjects) or projects involving deception.

In order for the IRB to waive or alter the informed consent process, the IRB must determine the following:

- The research involves no more than minimal risk to subjects
- The research could not be practicably be carried out without the waiver or alteration of informed consent
- The waiver or alteration would not adversely affect the rights and welfare of the subjects
- When appropriate, subjects will be provided with additional information about their participation (this mostly applies when a waiver of informed consent is being requested for a study that involves deception)

Ultimately, it is under the purview of the IRB of record to make a determination on whether a waiver of informed consent is appropriate for the study, depending on if the study meets specific criteria for the requested waiver. See the CW HRPP SOP manual for more details.