It is important to understand that there are additional considerations when conducting multi-site or collaborative research studies which engage Children's Wisconsin. It is important to be aware of these considerations and address them during the submission process so the study can be reviewed as efficiently as possible.

What are multi-site or collaborative studies?

The 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 investigator at each site. (Protocols that address the same research questions, involve the same methodologies, and evaluate the same outcomes are considered by the NIH to be the "same research protocol," even when variations due to local (research site) context exist. Per the NIH sIRB guidelines, non-exempt multi-site studies utilizing the same research protocol at each domestic (U.S) site are subject to sIRB regulations.)

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 as the participating sites. A multi-site project could be a clinical trial, an observational study, or a basic clinical research study.

A "**cooperative**" (or "**collaborative**") project involves two or more U.S. research sites where each site is conducting a different part of a research protocol under the direction/control of the lead PI. An example would be a non-exempt study where CW is the lead site and conducting the interaction/intervention with the human participants, but the analysis of the data is being done by is an external institution/collaborator.

Under NIH and Common Rule sIRB guidelines, both multi-site and cooperative research projects may:

- Require the use of a single IRB for oversight.
- Have a lead site/PI who receives the grant or contract from a sponsor and then establishes a subaward or subcontract to each participating site.
- Require authorization ("reliance") agreements to establish the contractual terms for IRB oversight and project management.

Any human subject research activities which engage institution in research will require oversight from an IRB. This oversight may be by each institution's local IRB OR it may be by a single IRB providing IRB oversight for all participating institutions.

Oversight by the local IRB

When CW is engaged in a research project, the MCW Pediatric IRBs will serve as our local IRB of record. There is already an IRB services agreement in place for any studies at CW that requires local IRB oversight. No new reliance agreement will need to be negotiated. These projects are submitted through eBridge, and will undergo CW HRPP local context review before moving on to the appropriate MCW pediatric IRB committee for review and approval.

Oversight by a single IRB

When CW is engaged in a human subjects research project and there is a request to rely on a single IRB **(that is not MCWs IRB)** for all participating institutions, a reliance agreement will be necessary. The reliance request and project details are also submitted through eBridge, with the selection in the application that there will be a reliance on another IRB. The request to rely and the project will also undergo CW HRPP local context review. While these projects are still submitted through eBridge, there is a slightly different process of review. More details can be found in the article regarding deferrals/reliance agreements **(this is forthcoming).**

ANY research that is taking place at CW and another institution - including MCW/Froedtert Hospital or Versiti - is considered a multi-site project.

CW and our campus partners (MCW/FH/Versiti) are legally separate and independent institutions. CW entered into the agreement to rely on the MCW pediatric IRBs as the primary (but not only) IRB for CW - but CW is still a separate legal entity.

This is the case even when CW and MCW/FH/Versiti are the **only** participating institutions, and the MCW pediatric IRBs are serving as the IRB of record. It needs to be clear in the submission exactly how the research will be conducted at CW:

- what research activities are taking place at CW
- what CW resources are being utilized

This also applies when an investigator would like to **add** CW as a site to an already approved research project, meaning CW will now be engaged in research that is already underway at MCW/FH/Versiti. Because CW and MCW/FH/Versiti are separate institutions, it is not sufficient to simply amend the existing project to add CW. If an already IRB-approved project is amended to include activities that now engage Children's Wisconsin, the Children's HRPP must ensure appropriate local context review and regulatory oversight of the pediatric population (e.g., oversight by an appropriate local site

investigator, involvement of coordinators knowledgeable about working in Children's space, review by the appropriate Pediatric Specialty IRB Committee). In certain circumstances, the project will require a separate submission for IRB review and approval.

If you are amending a study that now would engage Children's, contact the Children's HRPP Office for guidance before submitting the amendment in eBridge. Depending on the complexity of the study, guidance from the MCW IRB office may be needed as well. The Children's HRPP can identify what needs to be described in the application as well as any feasibility considerations and department sign offs that need to be in place prior to submission. The Children's HRPP will also ensure that the project will be reviewed by an appropriately constituted IRB with pediatric expertise.

For additional details, including what needs to be included in a multi-site protocol, please see the CW HRPP guidance Multi-Site Projects and Investigator Responsibilities

Before you begin the process of seeking IRB approval for multi-site or collaborative research, **contact the CW HRPP office** to discuss your situation and find the best solution. It is possible that not all collaborators are considered investigators from an IRB perspective, in which case multiple IRB review or a reliance agreement may not be necessary. We are in the best position to help you with all the considerations.