



MCW Office of Research Standard Operating Procedure

MULTI-SITE PROJECTS AND INVESTIGATOR RESPONSIBILITIES

Unit: Human Research Protections Program (HRPP), Office of Research

Applies to: Faculty and Staff involved in human research

PURPOSE:

To define the scope of MCW IRB oversight, to outline the responsibilities of investigators when participating in or leading multi-site research, and to describe information to be provided to the IRB regarding the oversight operations and practices which will be employed in the conduct of the multi-site project.

DEFINITIONS:

Clinical Trial: a research project in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Coordinating Site: The Coordinating Site will typically be the home site of the lead investigator for the entire project. For federally funded and/or FDA-regulated multi-site projects, the “primary awardee” or “grantee institution” will typically be designated as the Administrative or Coordinating Site. The MCW IRB requires the project to identify a nominal lead investigator by name and site when a multi-site project is being led or directed by two or more lead investigators (e.g. a leadership committee). The Coordinating Site is responsible for overall data management, monitoring and communication among all sites, and general oversight of conduct of the project.

Data Coordinating Site: Some projects designate one site to specialize in (among other things) receiving, verifying, and storing results from all sites.

Rely: Also known as “defer or cede.” An institution agrees to transfer oversight of a project under its jurisdiction to another IRB. MCW requires a signed Agreement to be in place prior to final IRB approval of the project. See IRB SOP: *Reliance Agreements for Multi-site Projects*.

Engaged in Research: An institution becomes “engaged” in human subjects research when its employees or agents (all individuals performing institutionally designated activities or exercising institutionally delegated authority or responsibility)

1. intervene or interact with living individuals for research purposes;
2. obtain individually identifiable private information for research purposes,
3. obtain informed consent from human subjects; or
4. receive HHS funds even when all activities are carried out at another institution or by employees of another institution. Determinations on MCW/FH/Versiti engagement in human subjects research are made by the MCW HRPP Director or designee.
 - a. Determinations on Children’s Wisconsin (CW) engagement in human subject research are made by the CHW HRPP Director or designee.

Multi-Site Project: The MCW IRB defines a multi-site project as a human subjects research project that will be initiated at more than one location other than or in addition to MCW. Examples of multi-site projects include:

- A project conducted at MCW, Children’s Wisconsin, and Versiti
- A project conducted at MCW and Marquette University.
- A project conducted at both Froedtert Hospital and the University of Wisconsin-Madison.

- A clinical trial conducted at forty different sites in the United States, even though the non-MCW sites may pursue IRB review independently.
- A project conducted at a social services agency in Milwaukee, or in a Milwaukee neighborhood.

Participating/Performance Site: A participating site is one at which staff are engaged in the conduct of research (see definition of “engaged”). A participating site is the actual place where the research activity takes place (e.g., clinic, hospital, community center). The participating site’s location may be different from the location where the IRB review takes place.

Reviewing IRB/IRB of Record: The IRB responsible for review of research involving a participating site. If the Reviewing IRB for non-MCW sites is the MCW IRB, a Reliance Agreement must be in place. See IRB SOP: *Reliance Agreements for Multi-site Projects*.

Safety Monitoring Site: Some projects designate a person, committee, or board (e.g. “Data Safety Monitoring Board”) to specialize in monitoring, reviewing, and analyzing adverse events and unanticipated safety/rights/welfare problems for the entire project.

MCW IRB Oversight:

The MCW IRB defines its scope of oversight jurisdiction to include:

- Human subject research activities conducted at MCW.
- Human subject research activities conducted or initiated by MCW employees or agents at any other site.
- Human subject research activities that make use of any MCW resources other than faculty or employee time commitment.

All projects meeting these criteria must be submitted to the MCW IRB for review and approval. If an investigator wishes MCW to rely upon a non-MCW IRB for review and approval of a project, consult the IRB SOP: *Reliance Agreements for Multi-Site Projects*.

Froedtert Health, Versiti and Children’s Wisconsin have assigned the IRB review and approval of human subjects research to the MCW IRB. In addition, Froedtert Health and Versiti have assigned decisions to defer IRB review to an external IRB to the MCW HRPP. Children’s Wisconsin HRPP maintains review and oversight of projects involving Children’s Wisconsin resources, and makes their own decisions when deferring to an external IRB is required and for a limited number of other projects. Questions regarding MCW IRB oversight jurisdiction should come to the MCW HRPP Office.

PROCEDURE:

Requesting reliance/deferral: When requesting that MCW/FH/Versiti rely upon another IRB for review of a project or that an outside institution, agency, or other entity rely upon the MCW IRB, an investigator must follow the procedures outlined in the IRB SOP: *Reliance Agreements for Multi-Site Projects*.

Sub-contracts or service agreements: When different institutions are conducting portions of a single federally funded non-exempt human subjects research project, a portion of the project on the MCW campus that is sub-contracted or which has a service agreement cannot be considered exempt. The entire project must meet one or more of the exemptions in order for the exemptions to apply to a sub-contracted or service agreement portion of a project.

IRB Submission

For multi-site projects, the IRB must review information about what research activities will be conducted on this campus and information about the entire project in order to understand how the MCW/FH/Versiti/CW investigators’ activities fit within the entire project. The breadth of information needed by the IRB is dependent upon the investigator’s role and will increase as the investigator’s responsibilities to the entire project increase. The list of required information below is in addition to that required for all new projects. See IRB SOP: *Submitting New Projects*.

In the following cases, the IRB application must provide a CV for the lead investigator from each site and a narrative in the protocol or protocol addendum that describes the resources available to the investigator:

1. MCW IRB is the Reviewing IRB for another site; or
2. The multi-site project is investigator-initiated and the MCW investigator is the lead PI for the entire project; or
3. The MCW investigator is lead PI for the entire project and the project is federally funded and/or FDA regulated.

1. For all multi-site projects, the IRB application must include:

- a. Identification of one lead investigator by name and corresponding lead site
- b. A description of research activities that will take place at MCW/FH/Versiti/CW
- c. A protocol that describes the entire project
- d. Operating or coordinating center procedure manuals to be used, if applicable
- e. If the same protocol is disseminated to all sites, a description of what parts of the protocol will/will not be conducted at MCW/FH/Versiti/CW, e.g. not enrolling minors when the project protocol includes adults and minors, not conducting a subproject as described in the project protocol
- f. The plan for continuing oversight of subject safety, name of individual at MCW/FH/Versiti responsible for evaluating and responding to subject complaints, plan for how the coordinating center will disseminate information to sites regarding UPIRSOs, new information, and changes in the project protocol or consent form

2. For projects where the MCW/FH/Versiti/CW PI is the Principal Investigator for the entire non-exempt project:

The scope of MCW IRB review will include

- a. the MCW campus site and MCW/FH/Versiti/CW project team activities;
- b. every subcontracted or component site and that site's staff; and
- c. the leadership, management, communication, and safety monitoring plans for the integrated whole.

Therefore, in addition to information listed in section 1 above, the eBridge SmartForm and IRB application should clearly describe the duties and activities of the MCW/FH/Versiti/CW PI as Principal Investigator of the entire project, including:

- a. Description of the Principal Investigator's responsibilities
- b. A list of all sites
- c. Description of research activities that will take place at MCW/FH/Versiti/CW and those that will take place at each outside site
- d. The name of the site where data will be aggregated, if there is a data coordination site
- e. Communication plan, including communicating changes to the protocol, interim analysis results, etc. to all performance sites
- f. Method for assuring all sites have and are using the most current version of the protocol and consent form
- g. Site where safety monitoring will be centralized (if applicable) with information about how to communicate with the committee/board.
- h. Monitoring plan appropriate to the nature of the project for receiving and evaluating subject complaints and protocol events, unanticipated problems involving risks to subjects or others and protocol deviations from performance sites
- i. Process for reporting all UPIRSOs from any site to appropriate institutional and federal officials, as appropriate
- j. If federally funded or FDA regulated, the MCW/FH/Versiti/CW lead PI must provide:
 - i. Documentation that each performance site has an FWA with OHRP on file or documentation of IRB approval at each site;
 - ii. Information regarding the engagement of any staff at any non-MCW campus site who is:
 - An employee of an institution without an FWA, or
 - Employed by an institution that has not executed a subcontract with MCW, or

- Not under the jurisdiction of an IRB that has approved their project activities.

3. For projects where MCW/FH/Versiti/CW is the Coordinating Site or other sites are relying upon the MCW IRB for review:

In addition to the information listed in sections 1 and 2 above, the eBridge SmartForm and IRB application should describe the duties and activities of MCW/FH/Versiti/CW as the Coordinating Site including:

- a. Description of the Coordinating Site's leadership structure and responsibilities
- b. Plan for ensuring the protocol and consent form have been reviewed and approved at each site before the project begins at that site
- c. Plan for assuring that informed consent is obtained in accordance with HHS regulations
- d. Plan for continuing oversight of the project including maintaining confidentiality of data, evaluating and responding to subject complaints, ensuring protocol compliance and data accuracy, evaluating problems and adverse events that arise during the project, communicating changes to the protocol, interim analysis results, etc. to all performance sites
- e. Plan for collection, management, and analysis of data from all sites
- f. When other sites are relying upon the MCW IRB for review, the SmartForm must include the PI and primary study coordinator from each relying institution as staff.

4. Community-based Multi-site Projects

- a. For projects for which MCW/FH/Versiti/CW PI is the Principal Investigator for the entire project, the IRB application should include:
 - i. List of all sites
 - ii. Description of research activities that will take place on the MCW/FH/Versiti/CW campus and those that will take place at community-based sites
 - iii. Description of who will conduct research activities on the MCW/FH/Versiti/CW campus and who will conduct those at community-based sites. These should be listed in the eBridge SmartForm as personnel
 - iv. A protocol that describes the entire project
 - v. Recruitment procedures at each site and who will be conducting these
 - vi. Procedure for obtaining informed consent at community-based sites, if applicable, and who will be conducting the process
 - vii. Name of individual at MCW/FH/Versiti/CW responsible for evaluating and responding to subject complaints and reporting UPIRSOs
 - viii. Plan for how new information and changes in the project protocol or consent form will be communicated to all sites
 - ix. If not federally funded, a letter of support from the community-based sites unless the site has already provided this document as part of an award application.
- b. For federally funded projects for which MCW/FH/Versiti/CW is the awardee or Coordinating Site, the IRB application must include all information listed in Section 1.
- c. For federally funded projects directed or initiated by an MCW/FH/Versiti/CW PI and for which a community-based organization receives federal funding via a sub-contract or other mechanism, the organization must have an FWA or contact the HRPP Office to discuss the possibility of an Individual Investigator Agreement. See IRB SOP: *Reliance Agreements for Multi-site Projects*.

5. Principal Investigator responsibilities when conducting multi-site projects

As with any project, the PI bears ultimate responsibility for safeguarding the rights and welfare of humans participating in the project, whether the PI of the entire project or of the local site only. See IRB SOP: *Responsibilities for Investigators Conducting Human Subject Research*.

6. Amendments, Continuing Review, and Reporting Responsibilities for Multi-Site Projects

Where there are multiple sites but the MCW IRB is reviewing for research conducted on the MCW campus only:

- a. The MCW/FH/Versiti/CW PI must submit study changes to the MCW IRB as outlined in the IRB SOP: *Amendments*.
- b. The MCW/FH/Versiti/CW PI must provide a report on the progress of the project to both the MCW IRB and the Principal Investigator for the entire project.
- c. The MCW/FH/Versiti/CW PI must report reportable events to the MCW IRB as outlined in the IRB SOP: *Requirements for Reporting to the IRB*.

IRB review has been ceded to an outside IRB:

- a. The MCW/FH/Versiti PI must submit local changes as outlined in the IRB SOP: *Reliance Agreements for Multi-Site Projects*.
- b. The MCW/FH/Versiti PI must report on the progress of the project to the Principal Investigator for the entire project and the reviewing IRB per their policies.
- c. UPIRSOs, serious and/or continuing non-compliance, and protocol violations must be reported to the reviewing IRB per their policies. The MCW HRPP Office must also be notified as outlined in the IRB SOP: *Reliance Agreements for Multi-Site Projects*.

MCW IRB is reviewing for outside institutions/agencies or MCW/FH/Versiti/CW PI is the Principal Investigator for the entire project:

- a. The MCW/FH/Versiti/CW PI must submit study changes to the MCW IRB as outlined in the IRB SOP: *Amendments*.
- b. The MCW/FH/Versiti/CW PI is responsible for gathering progress report information from the other sites, collating information, and providing both a status report for each site as well as a report on the progress of the overall project in the Continuing Progress Report to the MCW IRB.
- c. Reportable events must be submitted to the MCW IRB as outlined in the IRB SOP *Requirements for Reporting to the IRB* regardless of where the event occurs

7. Other Federal Agency Requirements

For projects which are supported by or receive funding from the Department of Defense (DoD) or a component of the (DoD):

- a. Investigators conducting multi-site research must indicate that a formal agreement (Memorandum of Understanding or other Agreement) between organizations which specifies the roles and responsibilities of each party has been executed.

REFERENCES:

N/A

SUPPORTING DOCUMENTS:

IRB SOP: Amendments

IRB SOP: Submitting New Projects

IRB SOP: Reliance Agreements for Multi-Site Projects

IRB SOP: Requirements for Reporting to the IRB

IRB SOP: Responsibilities for Investigators Conducting Human Subject Research

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