MCW Office of Research
Standard Operating Procedure

RELIANCE AGREEMENTS FOR MULTI-SITE PROJECTS

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

Applies to: Faculty and Staff involved in human research

PURPOSE:
Medical College of Wisconsin (MCW) Institutional Review Boards (IRBs) provide oversight for all human subject research conducted by MCW/FH/BCW faculty, fellows, residents, staff or students. This policy describes efficient review mechanisms available for multi-site projects when research conducted by Medical College of Wisconsin, Froedtert Hospital, or BloodCenter of Wisconsin personnel is subject to parallel oversight by the IRBs of other institutions.

MCW has a robust reliance system which includes established relationships, procedures, and forms that assist in an efficient reliance decision. Local investigators must follow the established procedures in order to assure the effectiveness of this system.

DEFINITIONS:
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.

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) (i) intervene or interact with living individuals for research purposes; (ii) obtain individually identifiable private information for research purposes, (iii) obtain informed consent from human subjects; or (iv) receive HHS funds even when all activities are carried out at another institution or by employees of another institution. The Director of the MCW HRPP or designee will make the final determination regarding engagement in human subjects research.

Federalwide Assurance (FWA): The only type of assurance currently accepted and approved by OHRP. Through the FWA, an institution commits to HHS that it will comply with the requirements in the HHS Protection of Human Subjects regulations at 45 CFR part 46.

Individual Investigator Agreement (IIA): An institution holding an OHRP-approved FWA may extend the applicability to cover two types of collaborating individual investigators when the project is federally supported: 1) collaborating independent investigator who is not otherwise an employee or agent of MCW, is conducting collaborative research activities outside of MCW, and is not acting as an employee of any institution when conducting the research; 2) collaborating institutional investigator who is not otherwise an employee or agent of MCW, is conducting collaborative research activities outside of MCW, and is acting as an employee or agent of an

institution that does not hold an FWA. This extension is documented using the Individual Investigator Agreement. The Director of the HRPP or designee will make the final decision regarding whether an IIA is appropriate for a specific case.

IRB Consortium: A group of IRBs that have established a working relationship with the goal of simplifying the IRB review process. In an IRB Consortium, a Master Reliance Agreement is signed and policies, procedures, and forms are developed which assist in implementing the reliance system.

Local PI: the MCW/FH/BCW investigator serving as the PI at the local site.

Master Reliance Agreement: An Agreement that is executed between multiple institutions in order to establish an IRB Consortium. The Agreement outlines expectations and common requirements that will be followed. The Agreement is between institutions and IRBs, not between collaborating investigators.

MCW IRB Oversight Jurisdiction: MCW defines the scope of oversight jurisdiction of the MCW IRB 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 research projects meeting these criteria must by 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, the procedures outlined in the sections below must be followed.

Froedtert Hospital and the BloodCenter of Wisconsin have assigned the IRB review and approval of Froedtert Hospital and BloodCenter of Wisconsin human subjects research to the MCW IRB. Questions regarding MCW IRB oversight jurisdiction should come to the MCW HRPP Office.

Multi-Site Project: A human subjects research project that will be initiated at more than one location other than or in addition to MCW. For examples of multi-site projects, see IRB SOP: *Multi-Site Projects and Investigator Responsiblities*.

Reliance Agreement/IRB Authorization Agreement/ Memorandum of Understanding: An Agreement executed between two or more institutions which transfers IRB oversight to another IRB in order to facilitate a single IRB review for a specified project or a group of projects. The Agreement is between institutions and IRBs, not between collaborating investigators.

Reliance System: A system developed by an HRPP Office which allows the institution to cede IRB oversight to another IRB or provide IRB review for a non-MCW institution. The system involves the use of policies, procedures, and forms that were developed to simplify IRB review for a multi-site project where at least one non-MCW site is relying upon the MCW IRB or where MCW is deferring IRB oversight to a non-MCW site.

Relying Site: The institution or agency that is relying upon the MCW IRB for review.

Reviewing IRB/ IRB of Record: The IRB responsible for review of research involving a participating site.

PROCEDURE:

1. All IRB reliance requests must be initiated with the proper MCW IRB Reliance request form and any required documentation.
2. All reliance requests are reviewed by MCW IRB Reliance in the order in which they are received.
3. PIs should be aware that there may be cases where a reliance request is denied. Therefore, the IRB encourages PIs to contact the MCW HRPP Office as soon as they can to avoid possible delays in IRB review.

Requests to rely on an outside IRB

1. The *Investigator Reliance Request Form* should be used when a MCW/FH/BCW investigator plans to participate in a multi-site project and would like to request that MCW rely upon a non-MCW IRB, The form must be fully completed and submitted via the instructions on the *Investigator Reliance Request Form*. All required associated documentation must be included with the initial email submission or the submission will be considered incomplete and will not be reviewed.
2. When the MCW HRPP Office is notified of a request to rely on another IRB, IRB staff will log the request, review the information, contact the PI for any additional information needed, and contact the appropriate HRPP Office regarding the proposed reliance request. Teams should allow 2 weeks for initial intake and review.
3. If the outside IRB has agreed to provide IRB review for the project, the local investigator must provide a signed *Investigator Attestation Form for Deferred Studies* to the HRPP Office. This form is required before MCW will finalize a deferral of IRB oversight to any outside IRB.
4. The local investigator must provide the IRB approval letter for involvement of this site when received.

Requests to rely upon the MCW IRB for review for a single site

1. The *Investigator Reliance Request Form* should be completed and sent to the MCW HRPP Office along with a copy of the protocol or narrative and proposed consent form, if applicable. These documents must be provided to the MCW HRPP Office before the request will be considered.
2. When the MCW/FH HRPP Office is notified of a request to serve as the reviewing IRB, IRB staff will review the information, contact the PI for any additional information needed, and determine if the request is appropriate. If there is a decision to move ahead with the request, IRB staff will contact the relying IRB directly.
    a. If an investigator wishes the MCW IRB to serve as the central IRB for multiple sites and the sites do not fall under an existing Reliance Agreement, the Director of the MCW HRPP or designee will be consulted in order to make a final determination regarding this request. This request is made via the *MCW as Single/Central IRB Request Form.*
3. If the MCW IRB agrees to provide IRB review for an outside institution, additional information in the eBridge SmartForm and in the protocol must be provided as described in the IRB SOP: *Multi-site Projects and Investigator Responsibilities*.
4. In addition to the above, the local investigator must provide the following information in the protocol regarding local context <u>for each site that is relying upon the MCW IRB</u>:
    a. the CV for each relying site's lead investigator must be uploaded in the eBridge SmartForm application.
        i. HRPP office may waive this requirement if the investigator is a faculty member of one of the insitutions within the SEWIC CTSI partnership.
    b. specific research activities to be conducted at that site
    c. available resources for each relying site's lead investigator must be described in the protocol or addendum to the protocol
    d. whether the relying site's research team will review records to determine eligibility

e. recruitment procedures to be conducted
f. consenting procedures to be conducted
g. confidentiality measures
h. if project involves a drug, device, or biologic, where these will be stored, who will dispense them, and who will manage them
i. for more than minimal risk projects, plan at the relying site for evaluating and responding to subject complaints and reporting UPIRSOs to the MCW IRB
j. age of majority in the relevant state (if minors will be recruited)
k. explanation of any state or local laws governing the conduct of research
l. any cultural concerns in the local community

Requests to initiate an Individual Investigator Agreement (IIA)

1. An Individual Investigator Agreement can be requested of MCW when <u>all</u> of the following are met:
   a. the project is federally supported and will be conducted under the direction and supervision of a local investigator;
   b. the collaborative investigator will be engaged in research activities outside of MCW, FH, or BCW;
   c. the MCW IRB is the reviewing IRB;
   d. non-MCW/FH/BCW research staff are employed by an institution that does not have an FWA, OR are not acting as an employee of any institution with respect to his or her involvement in the research; and
   e. the collaborating investigator is not affiliated with MCW or FH.
2. This mechanism does not apply if the collaborating investigator's institution is the primary awardee of federally-funded human subject research.
   a. the MCW investigator should contact the MCW HRPP Office in this case to discuss how to proceed.
3. In order to initiate a request for an Individual Investigator Agreement, the MCW investigator must complete the form *Request for Individual Investigator Agreement* and submit to the MCW HRPP Office along with:
   a. the protocol or the MCW IRB submission number (PROxxxx),
   b. the completed IIA form,
   c. evidence of the collaborating investigator's completion of human subject research protection (HSRP) training,
   d. and a letter of support from the collaborating investigator's institution if the collaborating investigator is an employee or agent of that institution. This letter of support must state that the institution is aware and supports the research activity taking place at their site. The letter of support is not required if a letter of support has already been provided with the grant proposal.

Consent forms for multi-site projects when a Reliance Agreement is involved

1. In all cases, the proposed consent form (if applicable) will need to be provided to the MCW HRPP Office.
2. **When the MCW IRB is the reviewing IRB**, the appropriate MCW consent form template must be used. Consent form templates can be found on the IRB website. Changes in the following sections may be allowed to accommodate local standards and requirements: compensation for injury, who to contact with questions about the project, and who to contact regarding rights and welfare of subjects. Template change requests may be required for these changes.
   a. the local investigator must provide the consent form for a non-MCW site for review and approval prior to use.
   b. the MCW IRB will review, approve and stamp the consent form to be used at the non-MCW site. This consent form must be used by the non-MCW site to enroll subjects.

    c. For information on consent form requirements, refer to *MCW IRB Reliance Consent Form guidelines*
3. **When MCW has deferred oversight to another IRB**, the MCW HRPP Office will work with the reviewing IRB to assure that the consent form used at this site includes language reflecting local standards and requirements.
    a. MCW expectation is that the consent form to be used locally includes select language on costs, compensation for injury, who to answer questions, and HIPAA.
    b. For information on consent form requirements, refer to *MCW IRB Reliance Consent Form guidelines*

Investigator Responsiblities

Local PIs must follow the IRB SOP: *Responsibilites for Investigators Conducting Human Subject Research* and IRB SOP: *Multi-site Projects and Investigator Responsibilities*. In addition to the responsibilities outlined in these policies, local PIs using the reliance system must also comply with the responsibilities listed below:

Investigator Responsibilities when the MCW IRB is the Reviewing IRB

1. Ensure that human subject research activities do not begin at any relying site until IRB approval is obtained in writing from the MCW IRB.
2. Submit an amendment to the IRB when adding a site to a project that has already been approved by the MCW IRB. The amendment should revise the protocol and SmartForm to include:
    a. addition of the site,
    b. explanation of research activities to be conducted at that site,
    c. and research activities to be conducted by employees of the site and where they will be conducted.
3. Include key personnel from the relying site in the SmartForm. If there are changes to key personnel during the course of the project, these changes should be reported to the MCW IRB.
4. Ensure that investigators at the relying site receive a copy of the IRB approval letter, approved protocol, consent form, and other documents (if applicable).
5. Notify investigators at relying sites of all MCW IRB determinations and communications, including those for initial review, continuing review, amendments and reportable events.
6. Upon request, provide access to records for audit or routine review by the MCW IRB.
7. The MCW/BCW PI is responsible for gathering progress report information from relying sites, collating information, and providing a status report for each relying site in the Continuing Progress Report to the MCW IRB. If the MCW/BCW PI is the Principal Investigator for the entire project, the progress report must also include the status of the overall project.

Investigator Responsiblities when a non-MCW IRB is the Reviewing IRB

1. Ensure that human subject research activities do not begin until IRB approval is obtained in writing from the reviewing IRB.
2. Ensure that all MCW, FH, or BCW institutional policies and requirements are met before initiating human subject research activities at that site. This includes Safety Committee reviews and approval from the Froedtert Hospital Office of Clinical Research and Innovative Care Compliance (OCRICC).
3. Ensure that all budgetary and contractural issues relevant to the conduct of the project are resolved before starting the research.
4. Ensure required agreements for data or specimen transfer (e.g. data use agreements, material transfer agreements, etc.) are in place prior to receiving or transferring data or specimens.

5. Adhere to the decisions and determinations of the reviewing IRB, including using only those project documents approved by the reviewing IRB.
6. Ensure that all project personnel at MCW/FH/BCW complete and maintain HSRP training as required by MCW.
7. Obtain and follow the most current IRB approved protocol. No changes may be made without approval from the reviewing IRB.
8. Unless the IRB determines that a waiver of informed consent or waiver of documentation of informed consent is appropriate, obtain and document consent using only the current IRB approved consent forms. Ensure that informed consent is obtained prior to initiating project procedures.
9. Report adverse events, unanticipated problems involving risks to subjects or others, and deviations from the protocol that occur at MCW, FH or BCW per the reviewing IRB policies.
10. Notify the MCW HRPP Office of serious or continuing noncompliance or unanticipated problems involving risks to subjects or others that occur at this site.
11. Report subject complaints that occur at this site to the MCW/Froedtert Hospital Research Subject Advocate.
12. Upon request, provide access to records for audit by the MCW HRPP or the reviewing IRB and notify the MCW HRPP Office of any non-MCW audit.
13. Provide IRB approval letters to the MCW HRPP Office when received.
14. Notify the MCW HRPP Office when the project closes at this site per the IRB SOP: *Project Closure*.

<u>Investigator Responsibilities when using an Individual Investigator Agreement</u>

1. Assure that the collaborating investigator has complied with all stipulations in the Agreement for reviewing *The Belmont Report*, the HHS regulations and relevant institutional policies and procedures for the protection of human subjects.
2. Assure that the collaborating investigator has completed HSRP training required by MCW.
3. When the IIA has been executed, submit an amendment to the MCW IRB to add the collaborating investigator to the project.

REFERENCES:

45 CFR 46

SUPPORTING DOCUMENTS:
IRB Form: Investigator Reliance Request Form
IRB Form: Request for Individual Investigator Agreement
IRB Form: Investigator Attestation Form for Deferred Studies
IRB Form: MCW as Single/Central IRB Request Form
IRB SOP: Responsibilites for Investigators Conducting Human Subject Research
IRB SOP: Multi-site Projects and Investigator Responsibilities
IRB SOP: Project Closure
MCW IRB Reliance Consent Form Guidelines
The Belmont Report

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