Marshfield Clinic

Deferring Ceding Review to an External IRB

1. SCOPE

1.1. System-Wide

2. DEFINITIONS & EXPLANATIONS OF TERMS

2.1. Cede / Defer IRB Review

- When an institution that has an IRB agrees to allow an IRB outside of its institution to act as its Reviewing IRB or IRB of Record. Review may be ceded/deferred for a single study or multiple studies.

2.2. External Collaborator

- Investigator or researcher who is not physician or staff member of Marshfield Clinic or St. Joseph Hospital engaged in research (See the document, "Determining Engagement in Research"). This is most often a student on site temporarily, or a researcher who is part of a multi-site research effort, and whose organizational Institutional Review Board (IRB) has deferred review to Marshfield Clinic Research Foundation IRB (MCRF IRB) via an IRB Authorization Agreement (IAA).

2.3. IRB Authorization Agreement (IAA)

- A formal, written agreement that allows an institution holding a Federal-Wide Assurance (FWA) to cede/defer IRB review to a second FWA-holding institution.

2.4. IRB of Record

- IRB that is responsible for the initial and ongoing review of a human participant research project, as designated by an executed IAA.

2.5. Lead or Overall Principal Investigator(LPI or OPI)

- Investigator who is responsible for the overall conduct of research on a multi-center study

2.6. Marshfield Clinic Principal Investigator(MCPI)

- PI of a given study, at the Marshfield site. There may be collaborating investigators at MC or other institutions

2.7. Participating Site:

- Any sites involved in conducting study procedures

2.8. Regulatory Point of Contact (POC):

- The person designated at each institution to make determinations regarding requests for his/her site to serve as the Reviewing IRB for a study or to defer/cede to an external IRB. POCs are likely to be individuals within an IRB office. Regulatory POCs are appointed at both the Reviewing and Relying Institutions/sites.

2.9. Relying Site:

- A site participating in a research study that has ceded IRB review

2.10 Reviewing IRB:

- The "IRB of Record" for the ceded sites (Relying sites) to which authority for review and oversight of a research study has been delegated.

2.11 Great Plains Collaborative (GPC)

- Network of medical centers in 8 states (**The Children's Mercy Hospital, University of Iowa, University of Kansas Medical Center, Medical College of Wisconsin, University of Minnesota, University of Nebraska Medical Center, University of Texas Health Sciences Center at San Antonio, University of Texas Southwestern Medical Center and University of Wisconsin-Madison, University of Missouri, Indiana University and MCRF)** focused on improving healthcare delivery through ongoing learning, adoption of evidence-based practices and active research dissemination. The GPC has an IRB reliance agreement which allows for eligible studies involving one or more GPC institutions to be reviewed by a single IRB of record.

2.12 Health Care Services Research Network (HCSRN) formerly HMORN

- Network of health care systems including MCRF collaborating in population-based research that measurably improves health and health care. The IRB reliance agreement allows for ceding to a single IRB of Record of data-only, epidemiological and health services research. It cannot be used for prospective biomedical research studies of human participants involving drugs, device or biologics.

2.13 Wisconsin IRB Consortium (WIC)

- Wisconsin Institutional Review Boards (**Aurora Health Care**, **MCRF**, **Medical College of Wisconsin**, **Univ. of Wisc. Madison**) collaborating among member institutions' IRBs in order to provide more effective and efficient oversight of multi-site human subject research protocols in Wisconsin and reduce costs and duplication of effort among the member institutions and affiliated investigators. The Consortium has established one agreement that allows any of the IRBs to serve as IRB of record.

2.14 National Cancer Institute Central IRB (NCI CIRB)

- Independent IRB of Record responsible for both study review as well as review of local context considerations for MCRF NCI-sponsored clinical trials**.** An NCI CIRB IAA is already in place.

2.15 Commercial Centralized IRBs

- Independent provider of regulatory and ethical review services for human research. MC has a Master Service Agreement (MSA) with **Western IRB - Copernicus Group (WCG or WIRB)** allowing for eligible industry sponsored drug and device clinical trials to be deferred to them as deemed appropriate by the MCRF IRB.

3. PROCEDURE BODY

This document explains the conditions under which Marshfield Clinic Research Foundation Institutional Review Board (MCRF IRB) will consider to defer/cede IRB review of human participant research to another IRB, how investigators may make deferral requests, the process of determination, and the policy and procedural implications of IRB deferral for Marshfield Clinic Principal Investigators (MCPI) along with the responsibilities the MCPI, MCRF IRB and External IRB. This procedure applies to research conducted at Marshfield Clinic, and at any of the Ministry Health Care hospitals. Decisions regarding requests from External Collaborators to defer/cede review to MCRF IRB are made according to the document, "Marshfield Clinic Research Foundation as IRB of Record."

3.1. IRB Review Requirement

a. See Human Participants in Research & the Human Research Protection Program for an explanation of when IRB review is required.

3.2. When Deferral/Cede Is Considered

a. The decision to defer/cede IRB review to another IRB will be individual to each situation, and at the discretion of the MCRF IRB Chair, and/or IRB Administrator. Factors to be considered include, but are not limited to:

- Affiliation of the Lead Principal Investigator;
- Level of engagement of Marshfield Clinic, or its employees or agents, in the research;
- Study population;
- Degree of risk of the research;
  - With rare exception, IRB review of greater than minimal risk research will not be deferred to a non-accredited institution. In rare cases, when the need for deferral is justified (e.g., prisoner research where MCRF IRB is not properly constituted to conduct the review), MCRF IRB will consider a deferral if the IRB to whom the review is to be deferred provides proof of human subject research standards equivalent to accreditation standards.
  - Minimal risk research will not be deferred to a non-accredited institution/IRB unless MCRF's Office of Research Integrity & Protections has the ability to access and review minutes of the reviewing IRB for the project in question.
- Location of various research activities;
- Nature of involvement of Marshfield Clinic patients or data;
- Plan to address issues of "local research context;" and
- Likelihood of ongoing deferral requests to a given IRB, such as a function of a consortium.

b. When review is deferred/ceded, an IRB Authorization Agreement (IAA) will be executed unless one already exists or an IRB Reliance agreement or Master Service Agreement (MSA) is already in place.

- Executing an IRB Authorization Agreement

- An IAA may apply to a single study, others to particular types of studies (eg. NCI Sponsored research), or to a group of studies.
- An IAA can be executed between two institutions or a group of institutions
- Non-standard IAAs, may require extended discussions between institutions and involve consultation with legal counsel.
- When there is an IAA executed the following must be documented in the IAA or in supporting documents

  Identifies and defines roles and timeframes for reporting to sponsors, federal and state applicable agencies serious adverse events, serious and continuing non-compliance, unanticipated problems involving risks to subjects or others, or suspension or termination of IRB approval.

  Clearly communicates expectations, including regulatory requirements, sharing of information between institution and the IRB, and a process for determining potential corrective/remedial actions in the event of non-compliance

  Communicates plan for sharing information about the site, the investigators, the sponsor, and the clinical trial between the institution and the IRB

  Identifies a process for responding to participant concerns and grievances, including coordination of communication to subjects

- Requires signature of Institutional Signatory Officials at both sites and possibly others (i.e. legal counsel, PI, etc)
- Once IAA has been signed by all required parties, the MCPI will receive an email and/or letter from MCRF IRB.

□ Master Service Agreement (MSA)

- Agreement which is generally already in place between MCRF and a Commercial Centralized IRB

□ IRB Reliance Agreement

- Agreement which is already in place between MCRF and Collaborative Networks (i.e. GCP, HCSRN)

c. MCRF IRB will generally not defer review of:

□ Gene transfer research;

□ Greater than minimal risk research and role of MC personnel is substantial (eg. Conduct of study procedures) unless it is an industry sponsored clinical trial;

□ Any MC personnel who has a COI that requires a management plan; or

□ Majority of participants are provided by Marshfield Clinic.

□ Research that is likely to qualify for IRB exemption

- The institution requested to defer to is not AAHRPP accredited

d. HIPAA Privacy Rule Considerations

- If a request for an alteration or waiver of the authorization requirement to use or disclose Protected Health Information under the HIPAA Privacy Rule is included in a deferred study, the IRB of Record is expected to also make privacy determinations.
- Alteration or Waiver provided should be documented

e. The decision to defer MCRF IRB review may be reversed at any point if the IRB Chair or IRB Administrator determines that the deferral does not adequately protect human research participants.

3.3. How to Request an IRB Deferral

a. Complete and submit to ORIP copies of the following for deferrals:

- MCRF IRB Request to Defer IRB Oversight form
- MCRF IRB Institutional Certification for IRB Deferred studies
- Protocol, Informed Consent, delegation log & other applicable study materials to make determination

b. Additional requirements may need to be followed as well, depending upon the deferral site

- NCI CIRB
  - Exception to above (section 3.3.a); only the IRB Institutional Certification for IRB Deferred studies and if applicable the Waiver of HIPAA Authorization, need to be submitted to ORIP.
- WIC
  - Review "How to Use WIC" on http://www.wicshare.com.
- GPC Researcher
  - Review Guidance for Researchers Using the GPC IRB Consortium document
  - Review Guidance for Relying on an External IRB: Frequently Asked Questions (FAQs)
- HCSRN
  - Complete and submit HCSRN Multi-Site Research Cover Sheet
- Commercial IRBs (Western IRB, Copernicus,)
  - Contact MCRF IRB Administrator first to discuss and be advised as to how to proceed
- Other IRB Deferrals
  - Contact MCRF IRB Administrator first to discuss and be advised as to how to proceed

3.4. MCRF IRB Deferral Determination Process

a. IRB Chair or IRB Administrator will review the submitted materials and make a determination if deferring/ceding is feasible. IRB Chair or IRB Administrator may request additional information from PI and/or staff, as applicable to assist in making the determination

b. Upon determination, notification to PI will be sent to the Deferring IRB of Record and to the PI. The IRB Institutional Certification form will also be included with the notification as well as any other specific site documents.

- If determination made by ORIP to cede, that IRB then becomes the IRB of Record for the designated research project and the MCPI is responsible to become familiar with and follow all applicable policies and procedures of that IRB. Particularly important are those which set forth reporting requirements.
  - The MCPI may then submit IRB application to deferred IRB, however may NOT begin that project at the site until approval has been received from the IRB of Record.
  - The MCPI must copy MCRF IRB on reports he or she makes to the IRB of Record of local unanticipated problems involving risk to participants or others, suspension of the research activity, instances of non-compliance, and suspension or termination of the research
- If determination was not given to cede by ORIP, MCPI should plan to follow MCRF policies and procedures for IRB submission and review.

c. Protocols deferred to a non-MCRF IRB for review may be included in the standard audit sample of ORIP and of the MCRF Office of Research Compliance.

3.5. Responsibilities of the MCPI, MCRF IRB, & External IRB

a. MC Investigator Responsibilities requesting and relying on an External IRB include; but are not limited to:

- Submit request to MCRF IRB to cede/defer IRB oversight to relying (external) IRB
- Obtain approval to cede from MCRF IRB and then proceed to submit initial application and changes in research to relying (external IRB) per site requirements
- Must NOT enroll individuals in research prior to review and approval by the relying (external) IRB
- Comply with the external IRB's policies and directives per the IRB Authorization Agreement as well as local institutional requirements where study is being conducted
- Ensure safe and appropriate performance of the research. This includes, but is not limited to ensuring the qualifications of research staff, monitoring protocol compliance, maintaining compliance with state, local or organizational requirements related to the protection of human subjects; providing a mechanism to receive and address concerns from local study

subjects and others about the conduct of the research; and investigating, and providing notification to the external IRB of any study specific incidence, experience, or outcome that rises to the level of an unanticipated problem and/or serious or continuing non-compliance.

- Communicate information about study progress and personnel changes to the reviewing (external) IRB via the mechanism established
- Comply with the determinations of the reviewing (external) IRB
- Use the most current IRB approved documents
- When responsible for enrolling subjects, will obtain, document, and maintain records of consent for each subject or subject's legally authorized representative as stipulated by the IRB
- Provide the external IRB person with the MCRF IRB Administrator's contact information.
- Ensure local institutional requirements in regard to study team training are met.
- Ensure local institutional reviews and sign-offs required to be in place prior to study activation are completed or obtained before beginning human subjects research.

b. MCRF IRB Responsibilities include, but are not limited to:

- Review Defer/Cede request and submitted study materials of an MCPI
- Use and follow Deferral SOP and Processing Form
  - Verify COI, CITI Training, Consistency Review completion
- Execute IAA or Reliance Agreement, if applicable
- Make determination to allow or not allow deferral/cede to external IRB
- Notify MCPI of determination via email and/or IRB letter and return signed Institutional Certification form
- Document reliance of an external IRB of Record in Research Database (ResDB)

c. External IRB Responsibilities include, but are not limited to:

- Conduct review of research according to all applicable regulations and laws including initial review, continuing review, and review of modifications to previously approved research.
- Conduct review of potential unanticipated problems, adverse events, and/or serious or continuing non-compliance.
- Provide notification to research staff and relying organization in writing of its determinations and decisions
- Make available relevant IRB minutes, IRB membership rosters, and standard operating procedures to the relying organization upon request.
- When appropriate, conduct on-site or remote post-approval monitoring or audits, unless delegated to the relying organization

- Maintain an IRB membership that satisfies the requirements of 45 CFR 46.107 and 21 CRF 56.107 and which provides special expertise as needed to adequately assess all aspects of each study.
- Promptly notify MCRF Institutional Official and the IRB if there is a suspension or termination of the external IRB's IAA to review a study
- Provide MCRF IRB, the contact person and contact information for the reviewing IRB.
- Maintain appropriate documentation per record retention policies, including and OHRP-approved Federal Wide Authorization (non-commercial IRBs) for human subject research

4. ADDITIONAL RESOURCES

4.1. References:
Marshfield Clinic Research Foundation IRB as IRB of Record
MCRF Investigators and Multi-Site Research

4.2. Supporting documents available:
- IRB Request to Defer IRB Oversight
- IRB Institutional Certification for IRB Deferred Studies
- IRB WIC Project Description and Review Request

5. DOCUMENT HISTORY

Version No.	Revision Description
1.0	New Document in Document Control transferred from the Policy & Handbook Library - #2683.4. Added new collaborative group definitions and processes (GPC, WIRB). Updated personnel titles in ORIP.
2.0	Title Change, Collaborator name change of HMORN to HCSRN. Revised types of studies allowable for deferral. Edited terminology for defer/cede processes to be consistent with other applicable policies. Add POC definition. Add info on IAA Execution. Add Deferral Request process. Add hyperlinks to IRB forms. Add Responsibilities of PI, and IRBs. Formatting changes
3.0	Change DCS file to match title change.

6. DOCUMENT PROPERTIES

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