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Standard Operating Procedures for Establishing a Single IRB (sIRB) Reliance and sIRB Submission Process

Contents

1. Purpose

This SOP is intended for cooperative research, multisite or multicenter trials involving human subjects for which Weill Cornell Medicine (WCM) investigators intend to serve as a participating or lead site, and for which research activities will occur at the WCM campus. Reliance on a single IRB typically occurs with: 1) multicenter, federally-funded research which require use of a single IRB, 2) Industry-sponsored clinical trials, 3) multicenter studies with NYP and CTSC partner institutions.

2. Abbreviations

BRANY	Biomedical Research Alliance of New York
COI	Conflicts of Interest
CTA	Clinical Trial Agreement
CTSC	Clinical & Translational Science Center
CWID	Center Wide ID
DUA	Data Use Agreement
HIPAA	Health Insurance Portability and Accountability Act
HRPP	Human Research Protection Program
HSS	Hospital for Special Surgery
IBC	Institutional Biosafety Committee
IRB	Institutional Review Board
FDA	Food and Drug Administration
MSKCC	Memorial Sloan Kettering Cancer Center
NIH	National Institute of Health
NYP	NewYork-Presbyterian
OHRP	Office for Human Research Protections
PAM-AR	Post-Approval Monitoring – Annual Report
PI	Principal Investigator
PRMC	Protocol Review & Monitoring Committee
sIRB	Single Institutional Review Board
SMART IRB	Streamlined, Multisite, Accelerated Resources for Trials IRB
SOP	Standard Operating Procedure
WCM	Weill Cornell Medicine
WIRB	Western Institutional Review Board
WRG-HS	Weill Research Gateway – Human Subjects

3. Background

On May 25, 2017, the National Institute of Health (NIH) issued an update to the "Final Rule" mandating that all U.S. domestic sites participating in cooperative research (where each site will conduct the same protocol) use a single IRB (sIRB) (see 45 CFR 46.114). The Final NIH Policy on the Use of a Single Institutional Review Board for Multi- Site Research applies to federally funded, non-exempt human subjects research. Career development, research training or fellowship awards are exempt. Implementation of the updated Final Rule was extended by NIH to January 25, 2018, and the policy is now in effect. In addition, this applies to awards from all federal agencies that are signatory to the Common Rule.

The WCM IRB operates under a distinct Federal Wide Assurance (FWA) with the U. S. Department of Health and Human Services, and maintains separate research administrative offices (i.e. IRB, sponsored research, etc.) as part of the institution's human research protection program (HRPP). Federally funded research activities conducted at or by personnel at all other WCM campuses or external institutions (affiliated or otherwise) are considered outside of the WCM IRB purview. As such, these activities must be governed by an IRB reliance agreement.

4. Establishing a Single IRB Reliance

4.1. Single IRB Reliance Agreement Establishment

A reliance agreement, also known as an IRB Authorization Agreement, is a document permitting WCM (the "Relying IRB") to cede review to an external IRB (the "IRB of Record") for a particular study involving human participants. In some cases, an external IRB will be the relying IRB and cede review to WCM as the IRB of record. For either case to occur, an agreement must be in place to delineate the roles and responsibilities of the involved parties.

The reliance agreement may pertain to activities of a single research study or it may pertain to multiple studies (e.g., a Master Reliance Agreement). In this way, only one IRB reviews and approves human subject research activities for all campuses and sites, avoiding duplicative review and regulatory oversight.

Both OHRP and the FDA permit an IRB the option to rely on the review of another IRB. While such agreements are required for federally funded cooperative research, the WCM IRB allows reliance for Industry Sponsored or Consortium trials that are multicenter or multisite upon request.

Each institution or campus involved in the research is responsible for ensuring compliance with their site's submission requirements for any ancillary reviews, including but not limited to review by the respective campus's Institutional Biosafety Committee (IBC) and Radiation Safety group. Research staff from each site must consult their own institutional policies to determine if additional requirements apply.

4.2. Existing Reliance Agreements

WCM IRB has executed reliance agreements with the following institutions to serve as the IRB of Record for certain non-exempt research (described further below):

Broad Reliance

- Cornell University Ithaca campus
- Memorial Sloan Kettering Cancer Center (MSKCC)
- Rockefeller University

WCM-NYP Oncology & COVID Research

- NYP Brooklyn Methodist Hospital
- NYP Queens

WCM Clinical & Translational Science Center (CTSC) Supported Research

- CUNY Hunter College
- Hospital for Special Surgery (HSS)
- Cornell University Ithaca campus
- Memorial Sloan Kettering Cancer Center (MSKCC)

WCM IRB has executed broad reliance agreements with the following commercial IRBs to serve as the IRB of Record when necessary:

- Biomedical Research Alliance of New York (BRANY) IRB
- Advarra IRB
- Western IRB (WIRB)

For trials not covered under these existing agreements, a request to establish reliance must be sought from the WCM IRB as early as feasible.

4.3. Request for Single IRB Review

When it has been established that a trial will utilize single IRB review, a determination must be made on which campus's or institution's IRB will oversee the trial conduct. To facilitate this process, both the WCM and External IRBs will collect and review basic information about the planned collaboration.

The WCM Principal Investigator (PI) or designee must initiate a request for IRB reliance via the WCM Qualtrics Portal or via email to singleirb@med.cornell.edu. It is suggested that the subject line indicate, "WCM-IRB Reliance Request, [Name of WCM PI/Name of External PI], [Study Title or Abbreviated Name]." The body of the email should contain the following information:

- Study Title and Abbreviated Title (if applicable)
- WCM and/or External IRB number(s)
- WCM and Overall PI Name(s)
- Funding source(s) (e.g. Federal, Institutional, Industry)
- Proposed lead IRB or participating sites if not yet known
- Briefly describe the role/involvement of WCM investigators and subjects (*Example: WCM investigators will receive and analyze the de-identified samples; WCM subjects will be approached for consent and blood draw.)*
- Availability for a brief follow up call or meeting

4.4. Determination of IRB of Record

Once a request for reliance has been received, staff from the WCM and External IRB(s) will jointly determine who will serve as the IRB of record for any given collaboration. A response from the IRB office will be provided within two business days of reliance request receipt.

The determination on which institution will serve as IRB of record for collaborative human subjects research will take into consideration the following:

- Awardee institution and/or PI for trial funding.
- Where research procedures are taking place, anticipated to recruit more, and/or anticipated to analyze data.
- The ability of the site or institution to serve as a HIPAA-covered entity and/or privacy board.
- Expressed preferences of the participating site investigators or IRBs.

Industry Sponsored multisite research will utilize a commercial IRB, unless an academic IRB has been identified and is in use.

4.5. Reliance Documentation

It is the responsibility of the WCM Principal Investigator or designee to complete the appropriate reliance form, obtain WCM review and approval of the reliance form, and obtain all local and external institutional signatures prior to study submission to the WCM IRB.

- To establish a new reliance that will cover more than one study, please contact the IRB office at singleIRB@med.cornell.edu to determine the appropriate documentation.
- For a study to use an existing reliance agreement, the WCM IRB Reliance Memo template should be used to document the specific research (single or multiple trials) to be covered and participating IRBs.
- For federally funded cooperative research (multisite or multicenter) WCM IRB has determined that participating sites must agree to utilize the SMART IRB Master Agreement for establishing reliance, unless a master agreement is already in place. It is preferred that the study team(s) involved initiate the reliance within the SMART IRB platform. If not feasible, the SMART IRB Acknowledgement Memo may be used.
- For multisite studies not utilizing federal funding, use of local reliance template will be required. The WCM Single Scope Reliance template, found on the IRB website, is the preferred documentation.

5. sIRB Submission Process

5.1. WCM IRB Review as the IRB of Record

Following a determination that WCM will act as the IRB of record for a particular collaboration, the WCM PI must complete the typical WCM IRB application using WCM's online protocol management system, WRG-HS, according to the guidance and directions of the WCM IRB.

Responsibilities of the WCM investigator or designee include:

- Submit all application materials to the WCM IRB, even in cases where the overall project PI is based externally, as a WCM "CWID" is required to access WRG-HS. As part of the IRB application submission, a copy of the executed reliance agreement or memo for the study must also be included.

- Provide a list of external investigators who will act as research personnel on the study as part of the application. This can be a Word or PDF document listing all non-WCM personnel, their respective roles and responsibilities on the study, email addresses, and noting their institutional affiliation.

- Ensure all persons on the list of external investigators complete an SSR (Study Specific Report) form disclosing their financial interests. These forms should be submitted to the WCM IRB with the application. The form can be downloaded at: https://research.weill.cornell.edu/conflict-interest-office.

- Ensure all persons on the list of external investigators have completed required training per WCM's policies, found here. WCM requires personnel on all human subject protocols to complete training in Good Clinical Practices, in addition to human subjects training. If external investigators will be conducting research procedures in WCM/NewYork-Presbyterian clinical space additional requirements must be met, including but not limited to HIPAA training, medical clearance, etc. External investigators will need to provide WCM's IRB with proof that they have completed these required trainings. Completion certificates must be attached in the personnel section of the IRB application.

While awaiting approval by the WCM IRB, the collaborating PI must complete and submit all required forms to their IRB for local context review, including providing the External IRB with summary information about the project, and details the specific roles and responsibilities of the local investigators.

Following approval, any reportable events (expected, unexpected or deviations) relating to the study should be reported to the WCM IRB, regardless of the affiliation of the investigators involved.

The Relying IRB reserves the right to place enrollment on hold, suspend or terminate the research activity or request additional protections at any external-based campus study site at any time. At such time, the External IRB or Institutional Official will promptly notify the WCM IRB of these actions.

5.2. WCM IRB Relying on a non-WCM IRB

Following determination that an External IRB will act as the IRB of record for a collaboration, the IRB of Record must provide approval for the following:

- Approve the research which includes WCM as a site
- The ICF document to be signed by WCM participants
- Any other research documents typically requiring IRB review.

After approval is received from the IRB of Record, the WCM PI must submit a "Non-WCM Review and Approval (Central IRB or Single IRB)" application in WRG-HS for local context review. If an existing study submitted as "Full/Expedited" is seeking to rely on an external IRB, a new study must be initiated in WRG-HS.

5.2.1. *Initiating Study at WCM*

WCM IRB must perform the local review and acknowledge the IRB approval before any research activities at the WCM site may begin. All WCM training and conflicts of interest requirements must be met, as well as ancillary committee reviews (e.g. PRMC, radiation safety, investigational pharmacy, etc.). It is the responsibility of the WCM PI to determine if additional agreements, such as Data Use Agreement (DUA) or Clinical Trial Agreement (CTA), are needed for the given collaboration.

5.2.2. *Informed Consent Documentation*

WCM requires use of approved consent form template language when enrolling subjects at our site (see Forms, Policies, & Guidelines) unless the IRB of Record explicitly requires use of their template. In such case, HIPAA and Subject Injury language must be used per the WCM template. Once the WCM consent form has been generated, review and approval must be obtained from the IRB of Record. Confirmation of IRB of Record approval and stamped ICF should be submitted to WCM IRB for local context review.

5.2.3. *Documentation of Local Context Review*

For studies using a reliance, the WCM IRB will provide an acknowledgment letter to capture local context review. Documents submitted will not receive a WCM IRB Stamp, but document name and version details will be indicated on the acknowledgement letter. If a local context survey is requested by the IRB of Record, the WCM PI or designee should

complete all applicable sections, and send to the WCM IRB for final review and signature at singleIRB@med.cornell.edu. To obtain a Conflicts of Interest (COI) determination for WCM investigators a submission in WRG-HS is required.

5.2.4.*Annual Renewals*

A continuing review by the IRB of Record will typically be required at least annually. The WCM PI should submit a continuing review for WCM IRB local context review within 14 days of receiving the approval from the IRB of Record. WRG annual renewal submission should include all approved documents and IRB of Record approval letter. A local context review will be performed, and an Acknowledgement letter will be provided. The expiration date of the WCM IRB local context approval will be determined by the IRB of Record's expiration date. The research activities may continue uninterrupted unless directed otherwise by the WCM IRB or the Institutional Official for Human Research Protections or the IRB of Record.

If the IRB of Record determines that continuing review is not needed, or that post approval monitoring is allowed, a PAM-AR should be provided to the WCM IRB. It is the responsibility of the study team to ensure timely submission, including all approved documents and IRB of Record approval letter. A local context review will be performed, and an acknowledgement letter will be provided. The expiration date of the WCM IRB local context approval will be determined by the IRB of Record's expiration date, if applicable.

5.2.5.*Amendments*

Any amendments to the protocol or ICF documents should first be approved by the IRB of Record. Within 14 days of receiving the approval notice, WCM investigators should submit the amendment to the WCM IRB through WRG for local context review. A local context review will be performed, and an Acknowledgement letter will be provided. The amendment to the research activity may be implemented upon receipt of approval by the IRB of Record unless directed otherwise by the Sponsor or Lead Institution. Please note that the IRB local context review may determine that the amended research is not acceptable for WCM, which may result in halting of the research project while a resolution is sought.

Any amendments to research personnel at WCM should first be reviewed and approved by the WCM IRB, unless stipulated otherwise by the IRB of Record in the reliance agreement or associated workflow documents governing the reliance. The WCM PI must

complete the typical WCM IRB application using WCM's online protocol management system, WRG-HS, according to the guidance and directions of the WCM IRB. Within 14 days of receiving the WCM IRB approval notice, WCM investigators should submit the amendment to the IRB of Record for review and approval as required.

5.2.6. *Reportable Events*

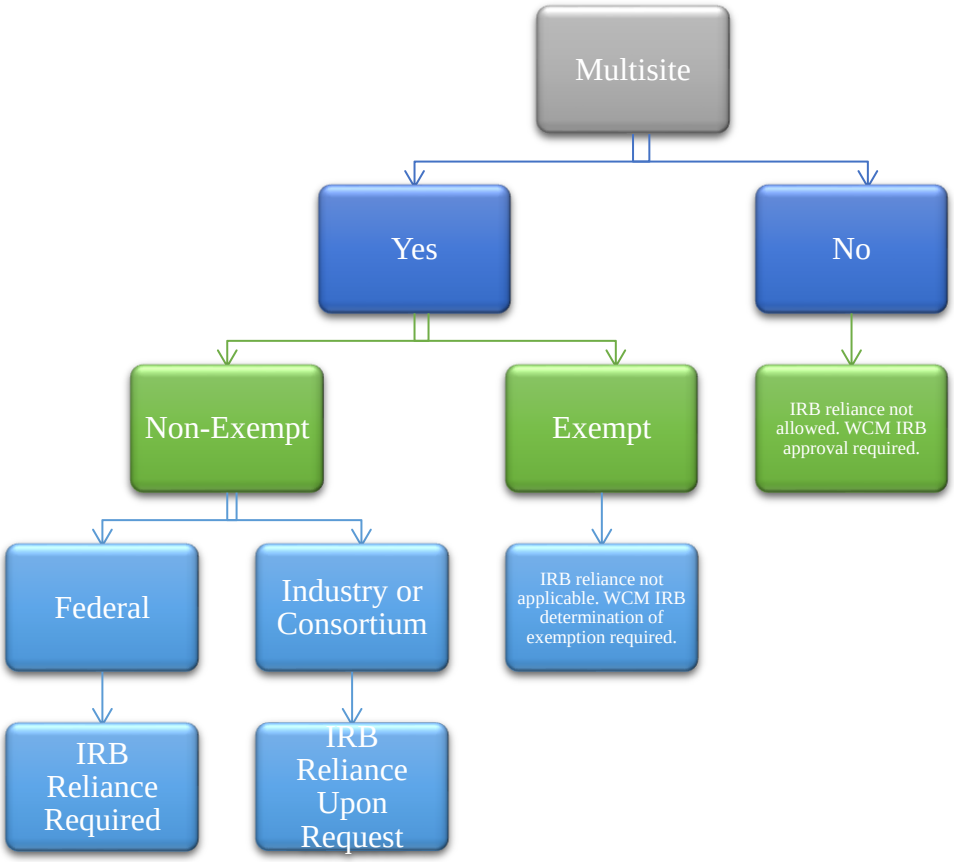
All reportable events must be reported to the WCM and External IRBs concurrently. WCM reserves the right to place enrollment on hold, suspend or terminate the research activity, or request additional protections at the WCM site at any time. At such time, the WCMC IRB or Institutional Official will promptly notify the lead site PI and lead IRB of these actions.

6. Further Information

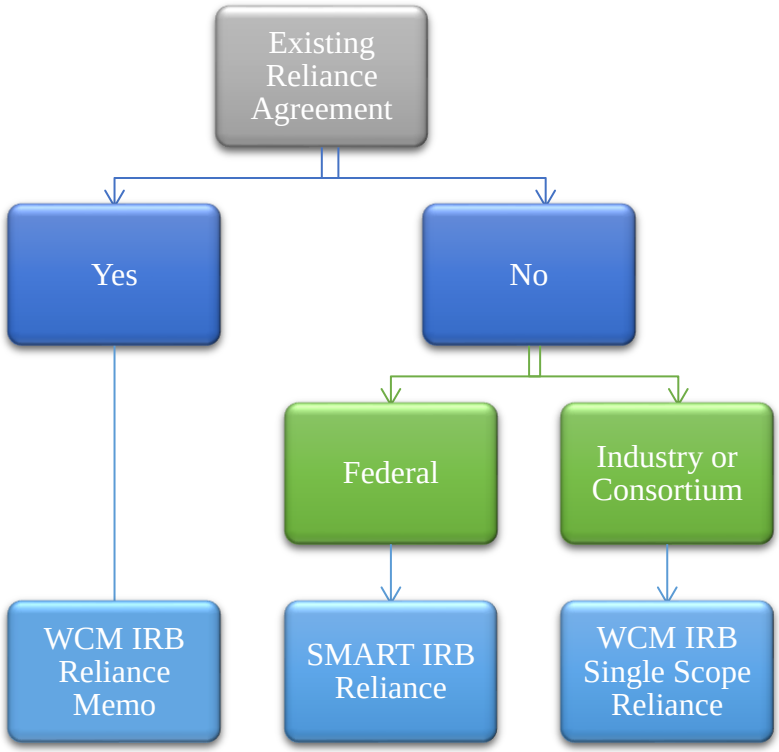
If you have questions about collaboration on human subjects research that are not addressed in this document, or wish to discuss a particular project, please contact singleIRB@med.cornell.edu.

7. Appendix

7.1.1. *Figure 1. Requirement for Single IRB Reliance Agreement Establishment*



7.1.2. *Figure 2. Required Documentation of IRB Reliance Agreement*



7.1.3. *Figure 3. Preferred Workflow for Single IRB Review and Submission*