Single Institutional Review Board (sIRB) of Record for Cooperative Research

Definitions:

Authorization Agreement – Also called the Reliance Agreement, which documents respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.

Multi-site research (cooperative research) – When the same protocol is being conducted at multiple locations (NIH definition) and/or when a single project involves more than one institution (45CFR46 definition).

Reviewing IRB (single IRB of record) – The IRB that will provide review for all or most sites participating in a multi-site study.

Relying Institution – the institution that has assigned an external Institutional Review Board (IRB) to serve as the Reviewing IRB under an IRB Authorization Agreement. Note the use of relying *institution* and not relying *IRB,* as the reliance agreement is between institutions.

Cooperative (multi-site) research conducted at Woman's

As of January 20, 2020, under 45CFR46, most federally-funded multi-site research must have a single Institutional Review Board (IRB) of record. The requirement for single IRB review applies to awardees in the United States and participating research sites in the United States. The requirement for single IRB review does not apply to organizations outside the United States. The awardee institutions are responsible for ensuring that authorization agreements are in place and that documentation is maintained.

Woman's IRB recognizes that for these studies a single IRB as chosen by the study sponsor or federal agency will be the IRB of record; however, all studies that are conducted at Woman's will be reviewed by the Research and Development Committee (R&D) for feasibility, scientific merit, and adherence to the mission of the hospital. The R&D Committee may also request local institutional IRB review by the full board or certain board members or consultants at the discretion of the R&D Chair in order to ensure protection of human subjects in research. This R&D review and possible subsequent local IRB review may not have regulatory implications but will be required in order for any study to be conducted at Woman's.

According to §46.114(b)(1):

> (b)(1) Any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.

A US institution that is engaged in cooperative research not federally conducted or supported, that has checked the box, would not be required to comply with the sIRB requirement in 114(b)(1). Woman's will use a single IRB of record, where possible, to avoid duplication of effort.

Woman's Hospital Research Center (WHRC) will maintain study records of all research studies conducted at the institution, regardless of whether Woman's IRB is the IRB of record or if Woman's is relying on an external IRB.

A single IRB of record is not required if more than single IRB review is required by law, or if a federal department or agency conducting the research determines that use of a single IRB is not appropriate.

For studies between Woman's and LSUHSC-New Orleans residents and faculty

For exempt studies:

LSUHSC-NO residents and faculty may rely on Woman's IRB for review and continuing oversight of human subjects research described as follows: any study conducted at Woman's involving LSUHSC-NO faculty or residents where Woman's IRB either

(i) determines the study is not humans subjects research or
(ii) determines the study to be exempt under applicable federal regulations.

Residents should submit any research proposals anticipated to qualify as exempt or not human subjects research to the WHRC for review.

For non-exempt studies with a **Woman's employee** as the Principal Investigator:

For non-exempt research conducted at Woman's with a Woman's employee listed as the Principal Investigator, Woman's IRB will be the IRB of record. The research proposal should be submitted to WHRC for R&D and IRB review. Woman's will use the SMART IRB Standard Operating Procedures (available online: https://smartirb.org/sites/default/files/SMART_IRB_SOP-090816.pdf) for delineation of responsibilities for the relying institution (LSUHSC-NO) and the reviewing IRB (Woman's).

For non-exempt studies with an **LSU employee** as the Principal Investigator:

LSUHSC-NO's IRB will be the IRB of record and Woman's will be the relying institution. Submissions should be sent to LSUHSC-NO with Woman's relying on LSUHSC-NO for review and oversight of the research.

When Woman's IRB is the IRB of record

For external sites: to request reliance on Woman's IRB

To request Woman's IRB as the IRB of record for an external site, the investigator at the external site should complete the Woman's IRB Reliance Application and submit it to WHRC.

Ideally, the SMART IRB Master Reliance Agreement will be used as the reliance agreement between Woman's IRB and the relying institution to outline the roles of each institution, if the relying institution is member of SMART IRB. If the external relying institution is not a member of SMART IRB, another reliance agreement acceptable to both institutions may be used.

Using SMART IRB as the reliance agreement

SMART IRB is not an IRB. SMART IRB is the name of a reliance agreement designed to streamline the reliance process between institutions and outline the responsibilities for each institution participating in the research project. SMART IRB was developed under an award from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH) to help facilitate multi-site human subjects research projects. Woman's joined SMART IRB as a participating institution; SMART IRB allows eligible institutions to join to rely on the IRB review and oversight of human subjects research by other participating institutions. A list of participating institutions can be found here: https://smartirb.org/participating-institutions/

SMART IRB is used at Woman's as the reliance agreement between institutions and for tracking the study progress, including submissions and reviews, and communicating the IRB reviews and approvals among sites.

SMART IRB Standard Operating Procedures (SOPs) will be followed for delineation of responsibilities from each institution. SMART IRB SOPs are available online: https://smartirb.org/sites/default/files/SMART_IRB_SOP-090816.pdf

Policies for Delineation of Responsibilities

Any studies using Woman's IRB as the IRB of record will follow Woman's IRB policies regarding review by the Research and Development Committee followed by IRB review. SMART IRB SOPs will be followed for delineation of responsibilities of Woman's and the relying institution. The responsibilities of Woman's as the IRB of record, the relying institution, the relying site study teams, and the overall PI and/or study team are outlined in the SMART IRB SOPs.

Woman's IRB will take into consideration any local context as provided by the relying institution in the Reliance Application, including institution-specific information for any informed consent documents. Woman's IRB will:

- document the reliance agreement among institutions
- confirm the flexible elements of the reliance agreement (e.g., auditing, reporting to external agencies, privacy considerations, etc.)
- collect study-specific local considerations from participating sites
- provide tracking tools for the lead study team/coordinating center to oversee site progress
- store and communicate IRB approvals and documents to participating sites

Each institution that is requesting reliance on Woman's IRB should submit a Woman's IRB Reliance Application and provide site-specific local context, local institutional requirements for investigators, and a study-specific reliance plan that is harmonized with the SMART IRB SOPs.

<u>As the reviewing IRB of record, Woman's IRB will be responsible for:</u>

- Performing initial review of new studies, discussing any issues with the Principal Investigator, notifying the Principal Investigator of any necessary modifications to the study, and making a final decision of approval or disapproval of the study. Conducting continuing review of the research (if required) and reviewing study amendments.

- Reviewing the R&D's assessment of conflict of interest and management of any conflicts as outlined in the reliance agreement

- Offering education in humans subjects research to investigators at relying institutions if such education is not available through their institution

- Providing template consent form(s), which indicate areas where the relying institution may add their required institutional language

- Making determinations regarding consent and authorization waivers or alterations

- Reviewing any protocol deviations, unanticipated problems involving risks to participants or others, notifying any relevant points-of-contact of the IRB's findings regarding unanticipated problems or research-related injuries or complaints, and reporting such events to the required entities (institutional officials, sponsor, OHRP, FDA, as appropriate). The relying institution will be given the opportunity to review and comment on the report before it is sent to federal agencies, such as OHRP and FDA.

- Suspending or terminating IRB approval when necessary and promptly notifying any relevant points-of-contact and the overall PI for the research and reporting any suspensions/terminations to appropriate federal agencies (such as OHRP and/or FDA). The relying institution will be given the opportunity to review and comment on the report before it is sent to federal agencies.

- Notifying any relevant persons of contact and the overall PI for the research any lapses in approval and any corrective actions plans

- Communicating with the investigators and, if applicable, the relying organization any decisions consistent with the reliance agreement, such as approval, disapproval, modifications, approval expiration dates, and continuing review notifications

- Obtaining any additional approvals from HHS when applicable when the research involves pregnant women, children, fetuses, or neonates

- Promptly notifying any relevant points-of-contact and relying sites, including the overall Principal Investigator, of any review and findings of serious or continuing noncompliance that may affect the conduct of the research and/or the rights, welfare, or safety of participants and reporting any serious or continuing noncompliance to the required entities (institutional officials, sponsor, OHRP, FDA, as appropriate). The relying institution will be given the opportunity to review and comment on the report before it is sent to federal agencies, such as OHRP and FDA.

- Notifying any relying sites of any allegation of research misconduct, confer with the relying institution's Research Integrity Officer regarding any misconduct report, and will handle the report as an unanticipated problem

- Making available any relevant IRB and HRPP records, including, but not limited to:

    - portions of the IRB meeting minutes that are relevant to the relying institution
    - the roster of the IRB membership
    - Woman's HRPP policies and procedures
    - approved protocols, consent forms, or other study documents
    - study-specific review and approval notifications
    - any other documentation as outlined in the SMART IRB SOPs

- Conducting periodic study monitoring, as applicable, and requesting any internal audit of the research, either conducted by Woman's IRB or the relying institution; notifying any relying sites of any audit findings and any findings regarding any federal audits or legal actions

- When conducting genomic research as the IRB of record, Woman's IRB will be responsible for meeting the additional requirements of the NIH Genomic Data Sharing Policy https://osp.od.nih.gov/scientific-sharing/genomic-data-sharing/

- Notifying any relying sites of any change or update to Woman's HRPP policies, FWA, IRB Registration, or accreditation status

- Maintaining an IRB membership that satisfies the requirements of 45 CFR 46 and 21 CFR 56 and provide special expertise as needed to adequately assess all aspects of each study
- Ensuring that IRB members receive orientation and continuing education on topics relevant to human subjects protection and there is adequate meeting space and sufficient staff to support the IRB's review and recordkeeping duties
- Notifying relying institutions of any changes in Woman's HRPP policies and procedures that might affect the reliance on Woman's IRB reviews or performance of the research and notifying any relying sites of any change or update to Woman's HRPP policies, FWA, IRB Registration, or accreditation status
- If Woman's ends its participation in the SMART IRB Agreement, or other Reliance Agreement as the IRB of record, informing all relying institutions of this change
- Continuing oversight of any activities if the reliance agreement is terminated during the course of the research until closure or mutually agreed transfer of the study.

The responsibilities of institutions relying on Woman's IRB are:

- When needed, provide a local context reviewer who has knowledge of the local research context and is able to review the informed consent form and related documents (e.g., authorizations for testing and release of medical records or donation of human specimens) to verify that these documents comply with applicable federal, state or local laws, institutional requirements, or Woman's IRB policies;
- Ensure the safe and appropriate performance of the research. This includes, but is not limited to, conducting the research as approved by Woman's IRB, monitoring protocol compliance, managing any major protocol violations, non-compliance, and any serious adverse events or unanticipated problems occurring at the institution, ensuring qualifications and training of research staff are commensurate with the research activity, and providing a mechanism by which complaints about the research can be made by local study participants or others;
- Provide evidence of adequate training of investigators in human subjects research;
- Promptly notify the Principal Investigator of its findings and actions with respect to any unanticipated problems involving risks to subjects or others or any research-related subject injuries or significant subject complaints that occurred at the relying institution—or that occurred at another relying institution if such events or actions relate to or may affect the conduct of the research or the safety, rights, or welfare of subjects participating in the research at the relying institution;

- Provide the names and addresses of local contact persons who have the authority to correspond on behalf of the institution;
- Maintain records of approved research as per institution policies;
- Maintain an OHRP-approved Assurance for human subjects research;
- Promptly notify Woman's IRB of events that may change the ability of the institution to conduct the research (e.g., suspension of the institution's FWA);
- Maintain a human subjects protection program compliant with 45 CFR 46 and 21 CFR 50 and 56;
- Maintain compliance with state, local, or institutional requirements related to the protection of human subjects; and
- Review and monitor individual and institutional conflicts of interest and provide the determinations and any management plans to Woman's IRB upon request.

Addition of investigative sites

Should a Woman's investigator conducting an approved protocol at Woman's wish to add an additional investigative site, this addition will be treated as an amendment to the current protocol and will usually be reviewed as a minor revision via expedited review. External sites should complete a Woman's IRB Reliance Application. The Research and Development Committee will review the amendment and forward their assessment to the Woman's Hospital Research Center, who will process this amendment for expedited IRB review. An addition of a site would be considered a minor revision if the addition would not materially affect an assessment of the risks and benefits of the study and would not substantially change the specific aims or design of the study.

Studies that involve life-threatening conditions, diseases causing serious morbidity, novel treatments for serious or life-threatening conditions, interventions with significant risk for serious adverse events, or studies that require data safety monitoring may require full board IRB review to add additional investigative sites. The IRB Chair may forward the amendment of an addition of an investigative site to the full board for review for any concerns that such a revision would not qualify as minor.

The IRB or IRB Chair may request additional information about the education and training of study personnel, the site's experience in conducting research, and safeguards for vulnerable subjects. In certain situations, the IRB may request that a site visit be conducted by the lead investigator.

External sites relying on Woman's IRB should submit any reports of serious adverse events, unanticipated problems, or noncompliance issues at their site directly to Woman's IRB.

HIPAA Privacy Rule

Woman's IRB will also make any required determinations regarding waivers or alterations to informed consent forms and HIPAA authorizations. HIPAA authorization language will be incorporated into an authorization form that is separate from the consent form. Woman's IRB evaluates the management of data and protected health information at the initial review and during continuing review of the study to determine that protection of participants is sufficient.

Conflict of Interest Management

Woman's Research and Development Committee will conduct conflict of interest analyses under Woman's HRPP Conflict of Interest policies with respect to disclosure and management of the relying institution's research personnel conflicts of interest. Woman's IRB will notify the relying institution of the R&D's and IRB's resulting determinations, prohibitions, and management plans, and any changes requested with regard to conflicts of interest. The relying institution may also propose any additional prohibitions or requirements to Woman's R&D and IRB for approval.

Notification of Decisions

The HPA and/or the study team will communicate with all sites involved and upload approved documents into the SMART IRB reliance platform, or send them directly to the sites electronically Notification letters will be sent to the PI regarding the outcome of the initial IRB review.

As the reviewing IRB, Woman's will use written communication to notify the relying institution(s) and/or PI of:

- determinations (exempt, expedited, full board) and review decisions (approval, disapproval, required modifications) regarding the specified study
- approved revisions and modifications to the study protocol or consent form
- lapses in IRB approval and any corrective action plans
- determinations and findings regarding unanticipated problems, adverse events, subject injuries, or subject complaints
- any determinations and findings regarding serious or continuing noncompliance and any required corrective actions
- any correspondence with federal agencies (NIH, FDA, etc.) and sponsors regarding the specific study, when necessary. The relying institution has the right to review and comment on the draft report and submit their own report in addition to any report from Woman's IRB.
- any results of for-cause or not-for-cause audits and their findings
- Any costs associated with review and entities responsible for payment (relying institution, sponsor, other third party)
- Interim results submitted by the investigator

When Woman's is the relying institution

When Woman's is asked to rely on another institution's IRB as the IRB of record, the investigator at Woman's should complete an External Reliance form and submit it to the Woman's Hospital Research Center for review. This submission should include the most recent version of the protocol, informed consent form, and any other study documents.

Approval from Woman's R&D is required before seeking IRB approval from an external IRB. Any questions regarding the reliance process can be directed to the Woman's Hospital Research Center (research@womans.org or 225-231-5275).

The Research and Development Committee (R&D) will review all reliance requests to determine if Woman's wishes to participate in the study based on adherence to Woman's mission, availability of resources, and scientific merit of the proposal. R&D will also review the request to evaluate reliance on the external IRB.

The reviewing IRB should provide a reliance agreement, documentation of the reliance arrangement, and an outline of the study-specific reliance plan (management of adverse events, conflicts of interest, etc.) that delineates the responsibilities of each institution. If the reviewing institution is a participant with SMART IRB, then the SMART IRB reliance agreement and SOPs can be used.

When reliance on an external IRB may be required

Specific external IRBs may be required in certain circumstances. These situations may include:

- Use of the Central Institutional Review Board for the National Cancer Institute (NCI)
- The funding entity requires use of an external IRB for multi-site research
- Federal regulations require the use of a specific IRB
- The principal investigator at another site mandates the use of a specific IRB as the IRB of record

When relying on a non-accredited institution

Woman's Hospital will rely on IRBs from AAHRPP-accredited institutions, except when such reliance is not possible. When relying on an external IRB from non-AHHRPP-accredited institutions, for minimal risk research, the reviewing IRB should assure that it will comply with applicable ethical standards and regulations (this assurance may be fulfilled by the reviewing IRB having a Federal-Wide Assurance on file with OHRP).

When relying on a non-accredited institution's IRB for greater than minimal risk research, Woman's may require additional oversight. Woman's and/or Woman's Research and Development Committee may:

- request to review the IRB minutes where the study was reviewed

- review the institution's SOPs for IRB review
- appoint a consultant from the Woman's HRPP for review of the study
- conduct not-for-cause audits of the study or monitoring of the IRB review process

To submit a study for reliance on an external IRB:

- Complete the External IRB Reliance application;

- Obtain any necessary department approvals for Woman's departments involved in the research; complete Department Approval Forms

- Complete a Material Transfer Agreement if any biospecimens are to be shipped off-site to the lead institution

- Submit a copy of the IRB Reliance Agreement from the reviewing institution

- Submit study-specific conflict of interest disclosures to Woman's Hospital Research Center;

- Ensure all local investigators are current on Woman's CITI training for human subjects research;

- Include: the current protocol, informed consent form with Woman's institutional requirements, and any other study documents.

  The consent form approved by the reviewing IRB for the main site must be adapted for use at Woman's and must conform to institutional requirements. To adapt a multi-site consent form for use at Woman's the following elements should be included:

  - Identification of Woman's as a research site;
  - Inclusion of a Woman's contact for emergencies or injuries;
  - The HIPAA language must include Woman's R&D and Woman's Hospital Research Center as institutions that will have access to PHI;
  - The name and contact information for the Woman's investigator needs to be provided for withdrawal of participation;
  - Contact information for the Woman's Hospital Research Center must be included for subjects' questions
  - Contact information for the Human Protections Administrator for questions regarding research subjects' rights

R&D Review of a Reliance Request

Woman's Research and Development Committee (R&D) will review the initial study for consideration of our site's participation, scientific merit, and adherence to the mission of Woman's. Additional review by directors/VPs of other departments, such as Health Information Management (HIM), Woman's Pharmacy, or other departments involved in the research, may be required depending on the nature of the study.

Once all required reviews are obtained, the decision to participate and rely on the external IRB will be communicated to the reviewing IRB and the Woman's study investigator(s). An institutional review will be conducted annually by the Research and Development Committee for these types of studies, including reviewing all on-site adverse events / unanticipated problems and enrollment status.

If the IRB of record is at an institution that is not a covered entity, the HIPAA Privacy Rule will still be followed at Woman's.

After Woman's Hospital Research Center receives all the required documents listed above, the reliance request with all supporting documents will be sent to R&D for review to determine:

a). that the study meets the mission and aims of Woman's Hospital
b). that adequate resources are available to conduct the study at this site
c). that the study has scientific merit and the protocol is sufficient to meet the aims of the study
d). that the reviewing IRB has sufficient expertise and/or experience to review the study and partner with Woman's in the protection of human subjects for this particular activity
e). that all concerns regarding the conduct of the study have been addressed and institutional responsibilities have been defined
f). that all conflict of interest concerns for Woman's investigators will be managed appropriately
g). that all Woman's investigators are current on CITI training in human subjects research
h). that the study consent form to be used at Woman's Hospital contains the institution's required elements

If changes are required to study documents, the Woman's investigator(s) will be notified of the requested changes and possible re-submission to the reviewing IRB may be required to re-approve updated documents. Once R&D review of the reliance request is complete and Woman's Hospital agrees to rely on an external IRB for review, the Woman's investigator(s) will be notified via written communication.

Investigator responsibilities when using an external IRB

Prior to IRB review, investigators should inform the reviewing IRB of the required site-specific consent form elements listed above and any applicable Louisiana state laws pertaining to the study (age of majority, etc.) if the reviewing IRB is out of state.

Investigators should submit to the Woman's Hospital Research Center:

- initial approval from the reviewing IRB
- study-wide amendments (protocol or consent form revisions)
- serious or continuing non-compliance reports
- any reports of serious adverse events or unanticipated problems
- any suspension or termination of the research by the reviewing IRB

Tracked changes of major modifications to the protocol or consent form should be submitted to the Woman's Hospital Research Center for review by the Research and Development Committee for assessment as to whether or not Woman's wishes to continue participation in the study and to ensure continued protection of subjects.

Any reports from the IRB of record or the sponsor of serious or continuing non-compliance, unanticipated problems, or serious adverse events should be submitted to the Woman's Hospital Research Center. Any suspension or termination of the research by the reviewing IRB should be immediately reported to the Woman's Hospital Research Center.

Upon receiving final agreement to rely on external IRB, the PI and study team remain responsible for ensuring all Woman's reporting requirements are maintained throughout the life of the study.

Responsibilities of Woman's investigators to the reviewing IRB:

1. Provide any information regarding local considerations (such as Louisiana's age of majority, HIPAA institutional requirements, local vulnerable population issues, etc.) to the reviewing IRB

2. Notify the reviewing IRB of any updates to our HRPP policies that may affect how research is conducted at Woman's

3. Comply with the determinations and requirements of the reviewing IRB

4. Cooperate with the reviewing IRB's responsibilities for initial and continuing review of the research, record keeping requirements, necessary reporting, and providing information regarding the conduct of the study in a timely manner

5. Disclose any investigator conflicts of interests upon initial submission to the reviewing IRB and promptly upon discovery of any new conflicts of interest according to the process agreed upon in the reliance agreement and comply with any management plans of these conflicts

6. Report to the reviewing IRB any proposed changes to the study for review prior to implementation (unless the changes must be implemented immediately to ensure the safety of participants)

7. Not to begin enrollment until approval from the reviewing IRB has been obtained and to obtain, document, and maintain consent records for participants, as required by the approved protocol

8. Report promptly to the reviewing IRB any unanticipated problems involving risks to participants or others, as outlined in the reliance agreement

9. Report promptly to the reviewing IRB any data safety monitoring reports that are received or any continued monitoring / audit results and to assist with the conduct of monitoring / audits as required by the reviewing IRB

10. Report promptly to the reviewing IRB any protocol deviations, noncompliance, or participant complaints, as outlined in the reliance agreement

Exceptions to HHS Single IRB of Record Requirement

For HHS-conducted or supported research, the Office of Human Research Protections (OHRP) has determined that the following research is exempted from the single IRB mandate:

1). Cooperative research conducted or supported by HHS agencies other than the NIH, if an IRB approved the research before January 20, 2020, OR

2). Cooperative research conducted or supported by NIH if either a). the NIH single IRB policy does not apply, and the research was initially approved by an IRB before January 20, 2020, or b). NIH excepted the research from its single IRB policy before January 20, 2020.