Ascension Wisconsin IRB Guidance & Submission Guide

IRB Reliance on the National Cancer Institute IRB

Ascension Wisconsin sites participate in the National Cancer Institute (NCI) Independent Model (IM) of review for Cooperative Group adult clinical trials.

This document provides background and guidance to PIs and study teams who work on studies delegated to the NCI CIRB.

For NCI CIRB site instructions, including submission instructions, see the Handbook for Local Institutions on the NCI CIRB website (https://ncicirb.org).

For directions on submission new studies or updates through the Mentor eIRB system, see the Mentor Researcher User Manual.

Contact the IRB office at IRB@ascension.org or 414-465-3134 if you have questions or problems.

Overview of the NCI CIRB Initiative

The Central Institutional Review Board (CIRB) Initiative is sponsored by the National Cancer Institute (NCI). CIRB is accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP) and provides expert IRB review at the national level prior to Cooperative Group distribution of the protocol to local investigators. The CIRB is composed of individuals who represent a broad range of oncology disciplines and may include oncology physicians, nurses, patient representatives, pharmacists, ethicists and attorneys. Ascension Wisconsin sites have a formal agreement with NCI CIRB, so investigators can participate in Cooperative Group trials and can take advantage of this single IRB review model.

In this Single IRB review model, the NCI CIRB serves as the IRB of record for eligible NCI cooperative group trials, but the AWRI IRB remains responsible for monitoring the conduct of the research at Ascension Wisconsin. All NCI CIRB submissions are screened by Ascension Wisconsin IRB Office staff to confirm that the research is appropriate for submission to CIRB, is consistent with local policies and guidance, and to confirm that the necessary NCI and institutional requirements (e.g., approved NCI *Annual Principal Investigator Worksheet about Local Context* form, CITI training, COI disclosure, HIPAA review) have been completed.

Criteria for Use of NCI CIRB

To take part in the CIRB initiative, principal investigators must be approved by the Ascension Wisconsin IRB and the NCI CIRB. In general, a NCI Cooperative Group clinical trial is eligible for CIRB review if the protocol is on the eligibility list, the PI is authorized by NCI CIRB and there are no plans to involve prisoners.

Opening a New Study with the NCI CIRB

Requests to open a new study using the NCI CIRB must be reviewed and acknowledged by the Ascension Wisconsin IRB Office before beginning submitted to the NCI CIRB.

The purpose of this local IRB review is to confirm that the study meets local requirements for eligibility for deferral to the NCI CIRB, HIPAA and foci reviews, confirm researcher training requirements, and to assist is tracking research occurring throughout Ascension Wisconsin.

Steps to request to open a study with NCI CIRB are outlined below. Please contact the IRB office with any questions at IRB@ascension.org or 414-465-3134.

STEP 1: Confirm staff and study eligibility with NCI CIRB

1. **Obtain a username and password to access the secured NCI CIRB sites** Investigators, sub investigators and research staff must complete annual registration through the Registration and Credential Repository at https://ctepcore.nci.nih.gov/rcr/lsUsersrc.action. The Oncology Research Coordinators have access to add, remove and update the CIRB and CTSU rosters, through the CTSU website.
2. **Confirm that the Annual Principal Investigator Worksheet about Local Context is approved by the CIRB.** To participate in an NCI CIRB study, the PI must have an approved "Annual Principal Investigator Worksheet about Local Context" on file with NCI CIRB. If this form is not already approved, open and complete Open a new Annual Principal Investigator Worksheet about Local Context through IRBManager.
3. **Verify that the study to be opened is on the CIRB menu by checking the CIRB Website.**

STEP 2: Opening a New NCI CIRB Study

1. **Complete the Study-Specific Worksheet About Local Context.** This should be completed by the lead researcher (or designee) via IRBManager. Instructions for completing the worksheets about local context can be found on the CIRB website.

   Complete the form but DO NOT click submit. Save a copy as a pdf file type.

2. **All study staff must also complete the institutional requirements**. This includes having a Mentor account, completing CITI training, and having a financial COI disclosure on file (completed before new individuals are added then at least annually).

3. **Submit a new study request to the Ascension Wisconsin IRB using the Mentor online system.** See the website and Mentor User Guide for instructions on how submit study in Mentor.

   Upload the following with your submission:
   - The draft Study-Specific Worksheet About Local Context completed in IRBManager
   - The current approved NCI CIRB study protocol
   - Most recent CIRB Approved transaction (e.g., Initial, continuing approval or amendment approval that list the expiration date)
   - NCI CIRB template consent
   - Local AW consent form, including the NCI CIRB-Approved boilerplate language. This is the only information that can be changed in the NCI CIRB approved consent form. The template language is in Mentor.
   - HIPAA Research Authorization, the standard stand-alone authorization should be used.
   - Any other approval required (Radiation Safety, IBC, etc.)

4. **If the Mentor protocol will cover multiple Ascension Wisconsin sites conducting the same protocol**, create one new protocol in Mentor as outlined above.

   In addition, on the main study page:
   - Select one Ascension site PI to be the main Ascension PI in Mentor
   - List all other Ascension site PI's as sub-I's
   - Select all local locations
   - List the enrollment goal as a total for all local locations
   - Upload a consent form for each local site
   - Upload a single HIPAA Authorization

   Of note, the IRB will issue a single approval letter for all sites. You can print the main page from Mentor to view sites/Investigators.

5. **The IRB office/reviewer confirms the Study Meets the Criteria for NCI CIRB Review** by verifying the following:
    - Applicable state laws and institutional requirements are met (e.g., radiation safety, institutional approval)
    - The study conforms to the Catholic Ethical and Religious Directives
    - Confirms the draft local consent form is accurate
    - Human subject protection training and financial disclosures are on file, and there are no financial conflicts of interest related to the study

    If there is an issue with any of the above the study will not be eligible for deferral to NCI CIRB. The Ascension Wisconsin IRB will inform the PI and lead coordinator through Mentor whether or not study meets criteria for NCI CIRB review.

6. **Submit the Study-Specific Worksheet About Local Context in IRBManager.** After receiving IRB acknowledgment, the coordinator can then submit the study to NCI CIRB. IRBManager will send an email prompting the PI to concur with submission. Approval notification will be sent from the NCI CIRB indicating study approval and that the CIRB is the IRB of Record for this study.

7. **Upload the NCI CIRB approval letter in Mentor using the NCI CIRB Update form.** The coordinator or PI must submit the final NCI CIRB approval letter to the Ascension Wisconsin IRB by uploading the letter with the NCI CIRB Update form, located on the IRB info page in Mentor. IRB staff will acknowledge the completion of the NCI CIRB approval.

Post Approval Responsibilities

The lead researcher remains responsible for the conduct of the study; post approval responsibilities include:

- Oversee the conduct of the research
- Monitor protocol compliance
- Maintain compliance with state, local, or institutional requirements for the protection of human subjects
- Investigate, manage, and provide notification to the CIRB of any study-specific incident, experience, or outcome that seems to rise to the level of an unanticipated problem and/or serious or continuing noncompliance.
- Subject complaints
- Breaches of confidentiality
- Annual progress reports
- When closing a study, submit closing report to the Ascension WI IRB, include a copy of CIRB Study Closure report

Submissions After Approval

The NCI CIRB is the IRB of record and conducts all IRB reviews.

However, the AW IRB must be informed of Study Staff and PI updates, Unanticipated Problems and Noncompliance, and Study Closure using the NCI CIRB Update form, located on the IRB info page in Mentor.

See additional on the following chart outlining the oversight responsibilities of the Ascension Wisconsin (AW) IRB and CIRB.

Submission type	NCI CIRB	AW IRB	Study site actions/details
Continuing Review	Obtain study renewal documents from the CTSU website.	These documents do not need to be submitted to the AW IRB.	When the CIRB posts the renewal documents, follow NCI CIRB SOPS to update local consent form to match the CIRB dates.
Cooperative Group Revisions posted on the CIRB website	These revisions have been approved by the CIRB.	These documents do not need to be submitted to the AW IRB.	Update all local documents, make the changes in your regulatory file and proceed under the revised protocol.
Cooperative Group Consent Form Revisions	These revisions have been approved by the CIRB.	These documents do not need to be submitted to the AW IRB.	Consent forms are considered approved for use once the study team has updated appropriately per the amendment and NCI CIRB SOPs. The approval date should be updated to match the CIRB approved consent.
Other Documents posted on the CIRB website (memos about drug shortages, letters, etc.)	All documents posted on the CIRB website have been reviewed and approved by the CIRB.	These documents do not need to be submitted to the AW IRB.	Include in your local regulatory file as appropriate.
Local document modifications (e.g., flyers)	These revisions are approved by the CIRB.	These documents do not need to be submitted to the AW IRB.	Submit to CIRB for review and approval. Include in your local regulatory file as appropriate.
Annual Principal Investigator Worksheet	PIs with an approved Annual PI Worksheet are contacted on an annual basis for updates.	The Annual worksheets do not typically need to be submitted to the AW IRB, unless specifically requested.	Follow the directions in the NCI CIRB Instruction Manual for Worksheet Completion in IRB Manager.
Changes to the HIPAA authorization or HIPAA noncompliance	These do not need to be reported to the CIRB.	Notify the AW IRB of HIPAA changes or non-compliance through Mentor using the AW IRB Update form.	The study team should use the current local approved HIPAA authorization form and ensure HIPAA compliance.
Revision that requires change of PI	These revisions are approved by the CIRB.	Notify the AW IRB of changes to the PI after CIRB approval through Mentor using the AW NCI CIRB Update form.	The PI must log into IRBManager and start an updated *Study-Specific Worksheet About Local Context and select "*Change of PI" as the reason.
Revision that requires change to the research personnel	Changes in staff are not submitted to NCI CIRB (other than the PI, outlined above).	Notify the AW IRB of changes to research staff through Mentor using the AW NCI CIRB Update form.	Study staff update the roster and regulatory file as appropriate.
Change in local sites	Notify CTSU of the addition or removal of the site.	Notify the AW IRB of the addition or removal of sites after CIRB approval through Mentor using the AW NCI CIRB Update form.	Include in your local regulatory binder as appropriate.
Addition of an Ascension WI Signatory Institution to a Mentor protocol already open at a different AW Signatory Institution	Open the new AW Study Site as usual following the NCI CIRB SOPs.	Notify the AW IRB following the instructions above to open a new study except- instead of creating a new study, submit the materials using the AW NCI CIRB Update form.	Include in your local regulatory binder as appropriate.
Unanticipated Problem or Noncompliance Events	Report to the NCI CIRB. The CIRB reviews, makes a determination, and reports to federal agencies as applicable.	Notify the AW IRB following the determination of the CIRB, by submitting a copy of the reports through Mentor using the AW NCI CIRB Update form.	The PI is responsible for reviewing local adverse events and noncompliance and reporting to CIRB if the event is determined to be a potential unanticipated problem or potential serious or continuing noncompliance.
Closing a NCI CIRB study	The NCI CIRB will acknowledge the closure.	Notify the AW IRB by submitting a copy of this report through Mentor using the AW NCI CIRB Update form.	Submit the NCI Study Closure form on the NCI website.

Local Language to be added to NCI CIRB consent forms for all Ascension Wisconsin sites

- Update the NCI CIRB consent form with the template text below, per the instructions provided.
- The only changes made to the ICF is the Approved Boilerplate Language below, unless specifically approved in the Study Specific Worksheet.
- Text should be formatted to match the font/size of the NCI CIRB consent form template.

Approved Boilerplate Language (v.11/21/19 approved by NCI CIRB 12/19/19)

Section: Header

Instructions: The local investigator name and contact information must be included in the header. If the NCI template includes this, no change is needed. If it is not included, insert the following information in a format consistent with the NCI template.

Boilerplate Language:
Principal Investigator:
[Name][Main Location] [Address] [Phone Number]

Spanish:
Investigador principal: [Name][Main Location] [Address] [Phone Number]

Section: What risks can I expect from taking part in this study?

Instructions: Reproductive risk language cannot dictate the use and/or methods of birth control, per the Ethical and Religious Directives for Healthcare.

Use all NCI CIRB language as is, except in the following cases:

- If the consent form includes language that indicates a subject can participate only if they use birth control, delete that language and replace it with statement 1 below.

    - If the consent form includes language that describes specific types of contraception required to used, delete that language and replace it with statement 2 below.

Boilerplate Language:
Statement 1: If you can have children you must agree to take actions to avoid becoming pregnant.

Statement 2: The following methods have been identified in the medical literature as being at least 99% effective in preventing pregnancy:

1) Complete abstinence from sexual intercourse
2) Use of two of the following methods in combination (a+b or b+c or a+c)
    a. a. Condom or occlusive cap (diaphragm or occlusive/vault caps) with spermicide
    b. b. Oral, injectable, or implanted hormonal contraceptives
    c. c. Tubal ligation or vasectomy (surgical sterilization) or intrauterine device or intrauterine system

You should discuss this matter thoroughly with your physician so that you are able to make an informed decision, and so you and your physician agree that you are taking appropriate precautions.

Spanish:

Statement 1: Si puede tener hijos usted debe estar de acuerdo en hacer todo lo posible para no quedar embarazada.

Statement 2: Los siguientes métodos son reconocidos en la literatura del campo médico como los más efectivos, por lo menos, con un 99% de efectividad en la prevención de embarazo:

1) Abstinencia sexual absoluta
2) El uso de dos de los siguientes métodos combinados (a+b o b+c o a+c)
    a. Condón o capuchón cervical (diafragma o capuchón cervical) con espermicida
    b. Anticonceptivos hormonales: oral, inyectable o implante
    c. Ligadura de trompas o vasectomía (esterilización quirúrgica) o dispositivo intrauterino o sistema intrauterino

Usted debería consultar de este asunto cuidadosamente con el doctor para poder tomar una decisión bien informada. De esta manera, ambos estarán de acuerdo de que está tomando las precauciones necesarias y adecuadas.

Section: Where can I get more information?

Instructions: Include any local contact information as required in the NCI CIRB template. In addition, if the template does not include a section for local contact information, add the following.

Boilerplate Language:

For questions about your rights while taking part in this study, call the Ascension Wisconsin Research Integrity and Protection Office at 414-465-3134.

Spanish:

Si tiene preguntas acerca de sus derechos mientras que participa en este estudio, llame a la oficina de Integridad y Protección de Investigación de Ascensión Wisconsin (Ascension Wisconsin Research Integrity and Protection) al 414-465-3134.

Section: Signatures

Instructions: Signature lines for the subject and person obtaining consent are required, while signature lines for the LAR and Witness/Translator should be included only if these individuals are expected to sign consent forms for the specific study. All signature lines must include a date and time. Use either English or Spanish language, for the respective consents.

If this information is included in the NCI CIRB template, nothing needs to be done. If it is not included, insert the information outlined below.

Wisconsin state law requires documentation of a physician investigator/ co-investigator discussion of risks, alternatives and benefits. Include the section below for all studies that include a treatment/ intervention.

Boilerplate Language:

Signature of Subject/ Firma del sujeto	Date	Time
Signature of Person Obtaining Consent/ Firma de la persona que obtiene el consentimiento	Date	Time
Signature of LAR/ Firma del RLA (Representante legalmente autorizado)	Date	Time

Signature of Witness/Translator/ Firma del testigo/traductor Date Time

Physician Investigator discussion:

This is to verify that the physician investigator/ co-investigator below has explained to and discussed with the subject or the subject's Legally Authorized Representative (if applicable) the availability of all alternate, viable modes of treatment and the benefits and risks of such treatments before the initiation of the research-related intervention.

Print Name of Physician Investigator/Co-Investigator

Signature of Physician Investigator/Co-Investigator Date Time

Section: Footer

Instructions: Add local version tracking (e.g. version, date, etc.)

Study Specific Worksheet Language

Any changes other than those outlined in the approved Boilerplate language above must be specifically approved in the Study Specific Worksheet for each study as applicable.

Examples of changes in the study specific worksheet may include the following:

Section: Who will see my medical information?

Instructions/Justification: If the research requires testing for communicable diseases that require reporting to the Health Department under Wisconsin State law, include the following statement. (WI Statues Ch. 252 Communicable Diseases, 252.05 Reports of cases)

Template Language:

This research requires testing for an infectious disease/condition. Under Wisconsin state law, if you are found to have a positive test result, the study team must report the test result to a state or federal health official.

Spanish:

Esta investigación requiere de una prueba de enfermedad infecciosa. Bajo la ley del estado de Wisconsin, si el resultado de la prueba es positivo, el equipo de estudio debe informarle a un encargado de sanidad del estado o federal.

Section: Optional Studies

Instructions/Justification: If the research includes an Optional study that is not being done at the site or is closed to accrual, insert the language below at the beginning of that section in order to clearly communicate to subjects that the section of the ICF is not applicable. All other text that is in the NCI template should remain the same.

Boilerplate Language:

This Optional Study is not offered at this institution or is closed to accrual.

Spanish:
Este estudio opcional no se ofrece en esta institución o está cerrado al devengo.