

AAH RSPP GUIDANCE

DEFERRAL/CEDING OF IRB OVERSIGHT TO AN EXTERNAL IRB

PURPOSE

This guidance addresses the Department of Health and Human Services (*DHHS*) (45 *CFR* 46.108, 45 *CFR* 46.114), Food and Drug Administration (*FDA*) (21 *CFR* 56.108, 56.114), Advocate Aurora Health System Policy and Advocate Aurora Health RSPP SOPs expectations regarding reliance on an external IRB.

Definitions of *Italicized words* can be found in the AAH RSPP Glossary.

GUIDANCE

What does Deferral of IRB Oversight mean?

In accordance with Advocate Aurora Health System Policy titled “Research Involving Humans or Their Identifiable Data or Biospecimens”, all *human subject research* conducted at Advocate Aurora Health must be either reviewed by Advocate Aurora Health’s IRB or formally *deferred/ceded* to an external IRB. Deferral of IRB Oversight is the agreement of an *institution* that has an IRB to allow an IRB outside of its *institution* to act as its reviewing/overseeing IRB, also called the *IRB of Record*. An *IRB Reliance Agreement* is a formal, *written* agreement between two or more institutions that is used to document the delegation of IRB review responsibilities.

Some IRB Reliance agreements are executed on a study-by-study basis; other IRB Reliance agreements are executed to allow for any study that meets the ceding requirements to defer to that IRB. **Contact the AAH RSPP early in the process if you are unsure if the IRB you intend to work with has an IRB Reliance Agreement in place.** The AAH RSPP can also help you determine if there are any specifics of that agreement that need to be considered. See later sections of this guidance document that provide information on what is included in the IRB reliance document as well as the responsibilities of the AAH research team/PI, AAH as the relying institution and the Reviewing IRB/IRB of record.

Note that the decision to defer Advocate Aurora Health’s *IRB review of research* may be reversed at any point if the *IRB Director*, *IRB Chair* or *Institutional Official* determines that the deferral does not adequately protect human research participants.

What studies can be ceded?

Studies not mandated for single IRB Review by federal regulation or funding agency policy may be ceded to an External IRB. The *IRB* oversight determination is made by the Advocate Aurora Health’s *RSPP*.

At AAH, to be eligible for ceding to an external *IRB* a study must meet one of the following criteria:

- * Federally funded
- No greater than *minimal risk*;
- The study involves an institutional conflict of interest;
- The research is a *phase III or IV* drug study or a *device* study where there is evidence of safety (i.e. not a pilot study).

* As of January 2018, NIH policy requires all sites participating in multi-site, non-exempt human subjects research funded by the NIH, to use a single Institutional Review Board (sIRB).

As of January 2020, multi-site human subject research studies sponsored by an agency that is a signatory to the Common Rule must use a sIRB.

Studies not meeting the ceding criteria above may be given individual consideration for ceding by the *RSPP* Director, in consultation with the *Institutional Official* as necessary. Submit an email requesting ceding to an external IRB (provide name of IRB) to the centralirb.office@aah.org email inbox. Make sure to include a copy of the protocol with the request. A decision on ceding of the research will be provided back to the submitter.

Note that:

- Treatment protocols, such as Expanded Access (Single patient or Intermediate Group Use) and Humanitarian Use Devices (HUDs) may also be ceded to an external IRB. The AAH RSPP will decide whether it is appropriate for the institution to cede these treatment protocols to an external IRB. To make a request to the AAH RSPP for ceding of a treatment protocol, complete and submit the *Request to Rely on an External IRB* form to the RSPP office (see form for details). A properly executed IRB Authorization Agreement is required for the ceding of a treatment protocol. Contact the AAH RSPP with questions.
- Studies *ceded* to an external *IRB* may be included in the standard Quality Review sample by AARI (CQAIR);
- Advocate Aurora Leadership (administrators, *Institutional Official*, Senior Vice President of Research) may review and approve/disapprove the conduct of any *research study* at Advocate Aurora Health Care, but no one may approve the conduct of the research at AAH if the study has not been approved by the external *IRBs*

What considerations does AAH take when deciding to cede IRB oversight to an external IRB?

Even when a study is eligible for ceding, AAH RSPP still needs to determine if relying on an external IRB is appropriate for the institution and the subjects participating in the research at AAH. If concerns arise during the RSPP consideration of the reliance request, the Institutional Official, in consultation with others if necessary, (Legal counsel, RSPP Director, IRB Chair, Research Compliance, Advocate Aurora Research Institute, and the research team) will make the decision relating to relying on an external IRB for oversight.

Considerations include:

- Does the proposed IRB of record have sufficient expertise and experience reviewing and overseeing research of a nature similar to the proposed study? For example, the study to be ceded to an external single IRB is one that targets a pediatric population. The proposed IRB of record should be experienced in reviewing pediatric research.
- Are there extraordinary risks to the research subjects?
- Are there any features of the protocol or the proposed subject population that pose special concerns?
- Can/Will the reviewing IRB accommodate the concerns of AAH?

What if AAH does not wish to cede IRB oversight to the proposed reviewing IRB?

If ceding to a single IRB is required by the federal funding of the research, and ceding is deemed not appropriate by the Institutional Official, an exception to the sIRB requirement may be sought. A compelling reason would need to be provided to the federal agency funding the research. If an exception is not granted, AAH would be left with the decision not to participate in the research.

If single IRB review is not mandated, the study could be reviewed by the Advocate/Aurora IRB.

Who is eligible to serve as External IRB?

If the research is federally funded, the naming of the IRB of record is done as part of the grant/funding process. If the research is not federally funded, any of the sites where the research is to be conducted may accept IRB oversight responsibilities. A commercial IRB may also be named as the proposed IRB of record.

The human research protections program (HRPP) of Advocate Aurora Health must adhere to the standards set by *AAHRPP* (Association for Accreditation of Human Research Protection Programs) in determining if AAH will defer oversight to a named external IRB. Consideration is given to whether the external *IRB* is 1) *AAHRPP*-accredited or 2) has an HRPP that has comparable ethical and protection standards to those proscribed by *AAHRPP* standards. This assessment may be accomplished by accreditation through an external organization (for example use of a checklist provided by *AAHRPP*), through OHRP's Quality Assurance Program, or other equivalent approach (for example the institution has been vetted by and is a member of the SMART IRB reliance system). When necessary, the AAH *RSPP* Director (or designee) will review the external *IRB's* policies and procedures to ensure they are equivalent to those of an *AAHRPP* accredited *institution*. An IRB assessment must have occurred or have been initiated within the past five years. If the proposed *IRB of Record* does not meet these standards, it is unlikely Advocate Aurora Health's *IRB* will consider ceding *IRB* oversight to that *institution*.

Can studies using a legally authorized representative (LAR) be ceded?

It is permissible to request reliance on an external IRB even when the study proposes the use of LAR. It will be the IRB of record who will ultimately decide whether the use of a LAR is appropriate in the research.

The Request to Rely on an External IRB form asks for information on the proposed use of LAR in the research. The AAH RSPP will consider state law and institutional policy when making the decision on whether the use of LAR is appropriate for AAH.

If the RSPP deems the use of LAR appropriate in the research, a letter will be provided to the PI/Research Team. This letter will outline the RSPP's considerations of local context issues (legal statutes or institutional policies) that must be addressed with the use of a LAR. It is the institution's expectation that this letter be provided to the IRB of Record by the study team during the deferral process.

Are Ceded Studies subject to AAH Quality Assurance Reviews?

Studies that are overseen by an external IRB are subject to the same quality assurance reviews as any other research study open at AAH. The reviews may be random or for cause. In addition, the RSPP Office will routinely conduct quality reviews on the informed consent documents approved by the IRB of record. Such reviews will ascertain if the AAH boilerplate consent/authorization language for ceded studies is being used.

Who addresses Privacy?

It is assumed that the IRB of Record will act as the HIPAA Privacy Board for the research study. If the IRB of record is not willing to serve as the Privacy Board for AAH, the research team will need to make this known in the Request to Rely form.

- Note that even if the external IRB acts as the Privacy Board for Research, the research team is required to follow AAH Privacy policies. This includes the **accounting of disclosures** of PHI. See AAH system policy on use and /or disclosure of PHI for research for details.

Although the AAH RSPP is willing to cede Privacy determinations that occur within the context of the research study, **ALL** preparatory to research determinations must remain with AAH. Submit the RSPP Preparatory to Research form with your Request to Rely on an external IRB.

What information needs to be provided to the RSPP to request ceding of your study to an external IRB?

A "Request to Rely on an External IRB" Form must be *submitted* to the Advocate Aurora Health's *RSPP* office to begin this consideration.

The following must be included with your completed Request to Rely on an External IRB application before the RSPP office will begin processing the request:

- Delegation of Authority log
- Copy of the current Study Protocol
- Authorization provided by the AAH Research intake process
- Device/Procedure Credentialing, when applicable

- BioSafety Committee Review for recombinant DNA or hazardous biologics, when applicable
- Radiation Safety Committee Review for radioactive materials, when applicable
- Completed Preparatory to Research form when screening/identifying potential subjects

NOTE that there is no need to include the proposed consent/authorization document with your Request to Rely submission to the AAH RSPP. See later sections in this document on how to create the consent/authorization document to be used to enroll AAH subjects.

Additionally, all key personnel taking part in the research and documented on the Delegation of Authority log must have completed the following:

- Current Human Subject Research training
- Current Research Significant Interest Disclosure Statement

The Request to Rely on an External IRB will be reviewed within the RSPP Office. An IRB Reliance Agreement [see “What is involved in securing an IRB Reliance Agreement?” section of this document] must be fully executed before you may submit your study to the external IRB. Only after receiving authorization from the AAH RSPP are you able to submit to the external IRB.

What should the PI/study team do after receiving authorization from the AAH RSPP to cede your research to an external IRB?

- Submit the study to the external IRB.
- Create a consent/authorization document to be used to enroll AAH subjects. Submit this to the external IRB. You should contact the external IRB to see if they already have a consent/authorization document to which you are able to add the local context language.
 - The AAH Ceded Research Boilerplate Consent/Authorization language (local context language) can be found on the AAH RSPP Website.
 - The AAH local context language (the AAH Ceded Research Boilerplate) must be included in the consent/authorization document **without revision**.
 - Most IRBs use a combined research consent/authorization document. However, if the external IRB wants a stand-alone research authorization to be used for the study the AAH Stand-Alone Research Authorization template (found on the AAH website) must be used **without revision**.
 - If the external IRB rejects any part of the local context consent/authorization language (i.e. AAH Ceded Research Boilerplate) you must inform the RSPP office. The RSPP will review the proposed consent/authorization document to determine if the revised document is appropriate to be used at AAH. Should the RSPP agree to the use of the altered consent/authorization document for the research study, you will receive written permission from the RSPP that must be provided to the external IRB.

- Note that you may be asked by the external IRB to provide the AAH local context language/consent boilerplate as part of their review of the study for AAH. If you are asked to do so, provide the appropriate AAH Ceded Research Boilerplate.
 - Most external IRBs will verify that consent/authorization document submitted to them includes this local context language. If they do not verify the inclusion of the local context language (i.e. AAH Ceded Research Boilerplate) it is **your responsibility** to ensure that this language is included in its totality.
- The AAH RSPP does periodic quality reviews of consent/authorization documents used in ceded research studies to ensure that the appropriate local context language is being used. If the AAH consent/authorization boilerplate language is **not** included the research study's approved consent/authorization document, and permission was not granted by the AAH RSPP to alter the consent/authorization language, this must be reported to the AAH RSPP as an **incident of noncompliance**. The noncompliance report should be submitted as indicated in AAH RSPP SOP titled *Noncompliance Submission Requirements* (found on the RSPP website).
- The Advocate Aurora PI may NOT begin the research project until approval has been received from the *IRB of Record*. This includes the *recruitment* of possible research *subjects*.
- Upon approval of the study by the external IRB, that IRB becomes the *IRB of Record* for AAH. The Advocate Aurora PI/research team is responsible to become familiar with and follow all applicable policies and procedures of the *IRB of Record*. Particularly important to note are those *SOPs* which set forth reporting requirements.
 - In addition to complying with the determinations and requirements of the external IRB, applicable AAH policies and all AAH IRB procedures, submit the following to the [RSPP Office](#):
 - Noncompliance—Report all events or occurrences meeting the AAH RSPP definition of Noncompliance - these can be serious, non-serious, continuing or non-continuing incidents. These events must be reported to the RSPP Office within 10 days of discovery of the event. NOTE: While the IRB of record may require only serious and continuing NC to be reported to them, this RSPP requirement is necessary to determine continuing NC.
 - UPIRSOs—Submit a copy of any unanticipated problem involving risks to subjects or others (UPIRSO) that is submitted to the external IRB if the UPIRSO occurred at an AAH site. Submit to the RSPP Office at the same time the event is reported to the external IRB.
 - Re-approvals/Continuing Review Notices—Submit notification from the external IRB of study continuation which includes the re-approval date and the approval period. These should be submitted upon receipt.

- Changes in key personnel—Submit proposed additions or removal of investigators or key personnel to the RSPP office prior to submitting the change to the external IRB (if necessary) using the *Changes in Key Personnel in Ceded Research* form. RSPP staff will verify that new key personnel have completed the required human subject research training, medical staff privileging (if applicable), and the significant interest disclosure process. Wait for RSPP Office notification before allowing personnel to engage in any research activities.
- Study completion—Submit a *Final Report* when the study is closed with the external IRB. This should be submitted within two weeks of study close out.
- Once initial approval is granted by the external IRB, a copy of the Initial Approval letter must be forwarded to the RSPP Office.

These notifications/forms must be submitted to the AAH centralirb.office@aah.org email box.

What should the PI/study team do if changes are made to a study AFTER the study has been ceded to an external IRB?

If any substantial information provided in the initial Request to Rely submission form changes, either to the study itself (e.g. a change to the study title, change to study funding source, or a change to subject population [study now allows enrollment of children]) or to the way the study will be conducted at AAH (e.g. the study team now intends to utilize LAR to consent patients, a change in consenting process is planned [e.g. inclusion of e-consent platform]) the PI/study team should complete and submit a new Request to Rely form, checking the “Substantial Modification” box. On the form, a rationale for the revision must be included as well as responses provided for the questions directly related to the change. You MUST wait to get the AAH RSPP authorization for these changes before implementing them in the study.

What is involved in securing an IRB Reliance Agreement?

The Advocate Aurora *RSPP* has an IRB Reliance Agreement (IRA) template available that takes into account the points outlined below. It is the preference of AAH that the Advocate Aurora IRA template be used as it has been vetted by AAH legal counsel. If another document is to be used as the Reliance Agreement, time will be needed for AAH legal counsel review of this document.

Execution of any IRB Reliance Agreement may require extended discussions between the involved institutions. Full execution of the agreement is required before your Request to Rely on the External IRB is authorized by the RSPP. Make sure to allow adequate time for the process to completed.

An IRB Reliance Agreement:

- may be executed between two *institutions* or a group of *institutions*.
- should identify any apportionment of *IRB* review responsibilities.
- should identify and define 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.
- should clearly communicate expectations, including regulatory requirements, sharing of information between *institution*, *investigator* and the *IRB*, and a process for determining potential corrective/remedial actions in the event of *non-compliance*
- should communicate plans for sharing information about the site, the *investigators*, the *sponsor*, the clinical trial and any relevant local context issues/factors between the *institution* and the *IRB*
- should identify a process for responding to participant concerns and grievances, including coordination of communication to *subjects*.
- requires signature of *Institutional Officials* at both sites.
- requires that a copy of the signed document be kept on file at both organizations and made available upon request to the Federal Office for Human Research Protections (*OHRP*) or any agency supporting the research.

The proposed reviewing IRB should be willing to provide AAH with information about its determinations and/or access to their minutes so that we may communicate questions or concerns. The authorization agreement may also provide access to additional documents.

Advocate Aurora Health currently has master reliance agreements with several external IRBs – Western IRB (WIRB)/Copernicus Group, Advarra, StrokeNet IRB, and National Cancer Institute (NCI) Central IRB (CIRB). AAH is also a participant in the SMART IRB National Reliance Initiative (SMART IRB). The SMART IRB reliance agreement can be used to facilitate the reliance process between numerous participating institutions. A list of signatory institutions can be found on the SMART IRB [website](#). In addition to these master agreements, individual reliance agreements may be executed between AAH and individual institutions as needed.

- Because of the flexibility in the SMART IRB reliance agreement, additional documentation must be executed/on-file to document responsibilities of the Reviewing IRB / Relying institution(s). Execution of the AAH SMART IRB Addendum Agreement is required for any reliance executed between AAH and SMART IRB participants.

Contact the RSPP office if you have questions whether there is an IRB reliance agreement executed between AAH and the external institution.

What are the responsibilities of the Advocate Aurora Principal Investigator (PI) in research ceded to an external IRB?

The AAH PI:

- Agrees to provide Advocate Aurora Health's RSPP contact information to the *IRB of record* for future correspondence.
- Provides the external *IRB* with any requested information about local context issues (including state law considerations, use of Legally Authorized Representatives in the study as determined by the AAH RSPP, etc.), resources and/or personnel at the research sites.
- Agrees that enrollment of *subjects* may not occur until study approval is granted by the *IRB of record*.
- Agrees to comply with the *IRB of Record's* policies and SOP's, directives and determinations.
- Agrees to comply with Advocate Aurora Health's system policies and all pertinent RSPP SOP's including the Post-Approval Responsibilities & Submissions SOP.
- Ensures that *Significant Financial Interests* of all study *key personnel* are reported and kept current per Advocate Aurora Policy (Conflicts of Interest in Research-Individual) and Advocate Aurora Health's *RSPP* (Initial Submission Requirements & Processes).
- Ensures that all study *key personnel* are current in their human subject research training requirements
- Agrees to cooperate with the *IRB of record* with regard to initial and *continuing review*, record keeping and reporting. All information requested by the *IRB of record* must be provided in a timely manner.
- Reports promptly to the *IRB of record* any proposed changes in the research (including *key personnel* changes) as directed by the *IRB of record SOPs*.
- Will not initiate changes in non-*exempt research* (including changes in the *consent* document) without prior review and approval by the *IRB of record*, except where necessary to eliminate apparent immediate hazards to the participants.
- Acknowledges that he/she is responsible for safeguarding the rights and welfare of each research *subject*. The rights and welfare of the *subject* take precedence over the goals and requirements of the research.
- Ensures 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 *IRB of record* of any study specific incidence, experience, or outcome that rises to the level of an *unanticipated problem* and/or serious or continuing *non-compliance*.
- Obtains, documents, and maintains records of *consent* for each *subject* or *subject's* legally authorized representative as stipulated by the *IRB of record* (as necessary per the study approval).
- Uploads a copy of the signed informed consent/authorization document(s) into the patient's electronic medical record as required by AAH Research Institute SOPs.

- Maintains and retains study records per IRB of record SOPs, AAH system policy, and AAH Research Institute SOPs.

What are the responsibilities of Advocate Aurora Health (AAH) as a relying institution in research ceded to an external IRB?

The following responsibilities are shared within the Human Research Protection Program (HRPP) at AAH.

- Prior to authorizing the deferral of IRB oversight:
 - verify current *Significant Interest Disclosure* and Human Subject Research training status for all study *key personnel*.
 - Review the study against the disclosed interests to determine if there is any relatedness. If potential relatedness is noted, the Research Compliance Department will determine if there is a Conflict of Interest.
 - Make appropriate and necessary *HIPAA* determinations.
 - Execute an *IRB Reliance Agreement*, if necessary/applicable.
 - Provide the external *IRB* (via letter/memo provided to AAH study team) with any state, local, or institutional requirements about the conduct of the research and the protection of *human subjects* (for example, *state law and institutional policy related to the use of a Legally Authorized Representatives (LAR) to agree to research participation on behalf of the decisionally incapacitated patient*).
- Acknowledge (via the reliance agreement) that AAH is responsible for safeguarding the rights and welfare of each research *subject*. The rights and welfare of the *subject* take precedence over the goals and requirements of the *research*.
- Comply with the *IRB of record's* requirements and directives, as well as responding to requests in a timely manner.
- Review reported incidents of noncompliance and unanticipated problems (per RSPP SOP) to ensure that AAH does not need to take interim action to protect the rights and welfare of the human subjects while the incidents are being evaluated by the IRB of record.
- Monitor the safe and appropriate performance of the *research* at AAH. This includes but is not limited to:
 - Monitoring ongoing research certification and potential conflict of interest of all key study personnel;
 - Monitoring *protocol* compliance;
 - Maintaining compliance with state, local, or institutional requirements related to the protection of *human subjects*;
 - Providing a mechanism to receive and address concerns from local study participants and others about the conduct of the *research*; and
 - Investigating, managing, and providing notification to the *IRB of record* of any discovered study-specific incidence, experience, or outcome that appears to rise to the level of an *unanticipated problem* and/or serious or continuing *noncompliance*.

- Participate in post-approval *monitoring* of the study/study conduct in addition to, or in cooperation with, the *IRB of record*.

What are the responsibilities of the IRB of record in overseeing AAH research?

- Maintain *IRB* membership that satisfies the requirements of 45 *CFR* 46 and 21 *CFR* 56 and provides special expertise as needed to adequately assess all aspects of each study. Provide membership roster to research team and Advocate Aurora Health upon request.
- Provide meaningful consideration of the ethical standards of the local community. This can be accomplished by:
 - Receipt of relevant local information in writing by individuals or organizations familiar with the local community, *institution*, and/or clinical *research*;
 - Participation of consultants with relevant expertise, or *IRB* members from the *institution's* own *IRB*, in the external *IRB's* deliberations;
 - Limited *review* by Advocate Aurora Health's *RSPP*, with that limited review focusing on issues that are of concern to the local community.
- Specify the contact person and provide contact information for the reviewing *IRB*.
- Provide approval documents/decisions to the research team and the AAH *RSPP*.
- Make available to AAH *RSPP* any relevant *IRB* minutes, Standard Operating Procedures, or other study documentation upon request.
- Conduct *review of research* according to all applicable regulations and laws (including state and local regulations/laws of the relying *institution*) 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 in *writing* to appropriate groups (*OHRP*, *FDA*, research staff and AAH) of its determinations and decisions.
- When appropriate, conduct on-site or remote post-approval *monitoring* or *audits*, unless delegated to AAH.
- Promptly notify the AAH *RSPP* if there is a *suspension* or *termination* of the *IRB of record's* approval of the study or the *IRB of record's* authorization to review the study.
- Maintain appropriate documentation per record retention policies, including *OHRP*-approved Federal Wide Assurance (non-commercial *IRBs*) for *human subject research*.

Please contact the AAH *RSPP* Office if you have any questions.

Resources

FDA Guidance for Industry: Using a Centralized *IRB* Review Process in Multicenter Clinical Trials (<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127013.pdf>)

OHRP Guidance on Use of a Centralized *IRB*
(<http://www.hhs.gov/ohrp/policy/protocol/cirb20100430.html>)