AAH RSPP GUIDANCE

Advocate Aurora Health (AAH) IRB as the IRB of Record for external sites

PURPOSE
To outline when the AAH may serve as the IRB of Record for external research sites, how a submitter can request that the (AAH) IRB serve as the IRB of record for an external institution or individual, the process for submission, and the responsibilities of AAH and the external site/institution.

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

GUIDANCE
Might the AAH IRB serve as the IRB for External Site’s?
The RSPP Office will make an individual study determination as to whether Advocate Aurora Health’s IRB has the capacity and ability to serve as the IRB of record for a non-Advocate Aurora site or individual engaged in human subject research. If you intend on requesting the AAH IRB act as the IRB of record for external sites, you must contact the RSPP Office as early in the study design process as possible, but in all cases prior to the submission of the study for AAH IRB oversight. Ideally the request to the RSPP Office for the AAH IRB to serve as the IRB of record should be made in writing (an email).

Typically the AAH IRB will only accept oversight for external sites when the AAH researcher is the lead researcher or AAH is the lead site of the no greater than minimal risk multi-site research, when the AAH researcher provides study-wide services, for greater than minimal risk research where the bulk of the research interventions are occurring at AAH facilities and the study involves only AAH and one or two other external sites. Factors such as RSPP resources, IRB expertise, and number of external research sites will be taken into consideration in making the final decision.

The following are examples of when it is more than likely that the AAH’s IRB will NOT serve as the IRB of Record:
- An industry sponsored or funded research study;
- The research study is greater than minimal risk, and the research interventions are not being conducted at AAH facilities;
- The non-Advocate Aurora investigator is not collaborating with an Advocate Aurora investigator on the research;
- The non-Advocate Aurora investigator is affiliated with a commercial, for-profit entity;
- The non-Advocate Aurora institution is unable or unwilling to provide appropriate local context information;
- The research takes place outside of the State of Wisconsin or Illinois;
• Multi-site research where Advocate Aurora is being asked to review the research for all or a large number of sites;
• Research in which an investigator has a conflict of interest (COI) and the researcher’s institution is not subject to federal requirements for significant interest disclosure and COI review or is otherwise unable or unwilling to manage the conflict;
• The research site does not have a Federal Wide Assurance with the Office for Human Research Protection.

The AAH IRB follows the ‘parent/child’ approach when overseeing external research sites. This means that, as often as possible, the study is first approved for AAH, and external sites are added via the modification/Change process. See more on this later in this document.

In all cases, when AAH IRB is serving as the IRB of record for external sites, it is expected that the AAH research team will act as the Lead Research team for the multi-site study. This requires the AAH research team submit all necessary Changes and continuing reviews (as necessary) to the AAH IRB, gather information on reportable events from all sites of the research and submit to the AAH RSPP/IRB, disseminate approval letters and copies of approved documents to the child/external sites, and be an all-around source of communication for the external sites to ensure that they are aware of and following AAH policies and RSPP SOPs.

You should always check with the external site’s IRB before attempting to add them as a research site in your study as they may not be willing to cede oversight to the AAH IRB.

How is a request made for the AAH IRB to serve as the IRB of Record for an External Institution or individual?

The AAH research team should notify/have a discussion with the RSPP Office prior to submission of the study for AAH IRB approval if at all possible, making it clear that they wish to have the AAH IRB serve as the IRB of record for external research sites/individuals. The RSPP Office would like to know of this possibility as early in the process as possible, so that a decision on IRB oversight for external studies can be made, as well as direct the study team in next-steps if this action is not possible.

A request for the AAH RSPP Office to act as IRB of record for external sites may be done via phone call to the RSPP Office or preferably via email (irboffice@aah.org). The information that will be required to be provided to the RSPP Office includes:
  • Title of study
  • Sponsor/funder of the study
  • The name of the AAH PI
  • AAH IRB study number (if already approved by the AAH IRB)
  • Number of non-AAH individuals or institutions being added to the research
• Whether the external institution/IRB has been contacted and has provided permission for the study to be ceded to an external IRB
• Brief description of the research interventions to occur at AAH
• Brief description of research interventions/activities to occur at the external site or by an external individual
• Agreement from the AAH PI for the AAH research team to serve as the Lead Research team in the study

The RSPP Director will consider the request and inform the AAH research team of the RSPP’s decision. Contact the RSPP Office if you have questions.

**What is the responsibility of the submitter when AAH agrees to serve as the Reviewing IRB?**

The external sites will be required to adhere to the IRB approved protocol and AAH RSPP SOPs. Once the RSPP has agreed to allow the AAH IRB to serve as the IRB of Record for the external site, it is the responsibility of the AAH research team to serve as the primary contact and resource for the external sites. The AAH research team will use the AAH IRB’s approved study documents (protocol, informed consent document(s), subject materials), along with input from the external site, to generate site specific ICF(s) and subject material(s).

The AAH research team must submit the following documents to the AAH IRB for the addition of each external institution:

• An AAH Change in Approved Research form (found on the RSPP website) noting the name of the external site and the name of the external site’s PI.
• “Local Considerations Worksheet-Institution” form (found on the RSPP website) if not already on file with the AAH RSPP Office (contact the RSPP Office if unsure). NOTE that it’s the responsibility of the external/relying institution to ensure that the information on file with the RSPP Office is current.
• “Local Considerations Worksheet-Protocol” form (found on the RSPP website)
• A copy of the Responsibilities/Duties Grid (found on the RSPP website) reviewed and agreed upon by the external sites. The Responsibilities/Duties Grid identifies and documents key communication roles and responsibilities between the Reviewing IRB (AAH), the Relying Institution and Relying site, and Lead (AAH) Study Team.
• A copy of the research consent/authorization document to be used at the external site (if applicable). The AAH IRB approved consent/authorization document should be used to create the external site document. For the most part, the consent/authorization language approved by the AAH IRB must remain without change in the external site’s consent/authorization document. The only changes allowed will be the local context consent language documented in the Local Considerations Worksheet-Institution (noted above) submitted or on file with the RSPP. This external site local context consent information should be included in the consent document as ‘tracked’ changes.
  o The Institution worksheet will also outline if the AAH IRB is to act as the Privacy Board for the external site. If the AAH IRB is serving as the Privacy Board, the
authorization language included in the AAH IRB approved consent document should remain without revision.

- If the external site(s) or their responsibilities are not already clearly indicated in the AAH IRB approved protocol, the Change should include an update to the protocol.

*NOTE that the external site does not need to provide a delegation log listing key personnel and roles for the external site. However, the AAH research team as the lead site should collect and retain a list of all research personnel conducting the research at all sites as you may be requested to provide that information to the AAH IRB at some point.

It is the responsibility of the external site/institution (per the executed IRB reliance agreement) to ensure that key personnel from that site/location are appropriately trained and have completed their institution’s COI process prior to being added to the study.

**What is the role of the AAH IRB in reviewing the Change to add an external site?**

The addition of external research sites can be provided expedited review. The Expedited Reviewer will review the external site’s information provided in the materials that accompany the Change form. If the expertise of the external sites appears appropriate to be included in the research study, the Expedited Reviewer may approve the addition of the site to the study. If the Expedited Reviewer has concerns about the appropriateness of the external site to the research study, more information may be sought, or the Change escalated to the convened board for consideration. The Expedited Reviewer may not disapprove the Change him/herself.

Prior to issuance of final approval of the Change, the RSPP Office will ensure that the IRB Reliance is appropriately executed. This may require execution of an IRB Reliance agreement between AAH and the external site, or completion of a SMART IRB Indemnity & Insurance addendum if the external sites is part of the SMART IRB Network. Execution of one of these documents may take extra time to complete – so plan your research study initiation accordingly. Contact the RSPP Office with questions.

Following Change form approval - including final execution of the IRB reliance between AAH and the external site - the AAH (Lead) site will receive a copy of the approved Change form, the agreed-upon Responsibilities/Duties Grid, and a letter documenting the reliance of the external institution on the AAH IRB for oversight of the study. These documents should be retained by the Lead Site as well as forwarded to the external site for their records. The external site may be required to provide copies of these documents to their IRB office depending on their institutional policies.

**Do key personnel from the external sites need to be documented on the AAH Change form?**

No. However, per the executed IRB reliance agreement between AAH and the Relying institution, key personnel from the relying site must have competed the HSR training and COI requirements of their home institution before conducting research activities. Failure of any key personnel to be current in HSR training and COI reporting is an instance of noncompliance reportable to the AAH RSPP per RSPP SOP #5.
While AAH IRB oversight of external key personnel delegation is not required, it is expected that the AAH (Lead) research team:

- keep a current, accurate record of key personnel from all external sites and their roles in the research should this information be required by auditors, the AAH IRB or the Relying Institution.

- changes in key personnel for the AAH research site(s) be submitted to the AAH RSPP on an AAH RSPP Change form. This will allow the RSPP to check for completion of HSR training and COI completion for these individuals.

**What is a Reliance Agreement?**

When AAH IRB agrees to serve as the IRB of Record, the responsibilities of AAH and the Relying Institution are outlined in an agreement executed between the parties. This is the Reliance Agreement.

This agreement ensures compliance of both parties with applicable regulation and protection of human research subjects. In cases where the written agreement allows for flexibility in the execution of institutional responsibilities (for example the SMART IRB reliance agreement), the AAH RSPP will document specifics in separate documents (for example the SMART IRB Insurance and Indemnification Addendum, Responsibilities/Duties Grid, etc). These ancillary documents establishing the responsibilities of the parties involved in the reliance and must be finalized before IRB approval will be issued.

**What are the responsibilities of the AAH IRB when agreeing to serve as the IRB of Record for an external site?**

The AAH IRB is responsible for:

- Reviewing external site-specific materials, including a completed Site-specific submission form, subject materials and consent/authorization document(s).

- Determining when local context issues are pertinent to the conduct of the study at the external site.

- Provide continuous oversight of the study, including external research sites.

  (i) Conduct continuing review of the study at intervals appropriate to the degree of risk in such Study, but not less than once per year, if applicable under the revised Common Rule 2018.

  (ii) Suspend or terminate IRB approval, as necessary;

  (iii) Review unanticipated problems or risks to participants or others;

  (iv) Review incidents of serious or continuing non-compliance;
(v) Make available relevant IRB minutes to Relying Institution upon request;

- As determined appropriate by AAH, conduct quality assurance reviews, for cause and not-for-cause post-approval monitoring/audits of research conducted at the external site. By submitting to the AAH IRB, the external site agrees to allow post-approval monitoring or auditing consistent with FDA regulation (21 C.F.R. § 56.109(f)) and FAQs.

(i) With reasonable advance notice, external sites shall permit:

a. site visits by the AAH IRB or designees;

b. remote monitoring by AAH IRB or designees;

c. monitoring by the site’s quality/auditing specialists (if available) with reports sent to the AAH IRB.

Site monitoring may involve meeting with the Principal Investigator and Site staff. Monitoring activities may include review/questioning of the following: the conditions surrounding the conduct of the study, study records, informed consent process/documents, the attitudes of the community from which study subjects are selected, the current status of the study, subject complaints, noncompliance, reports of unanticipated problems, high drop-out rates, or any other factor that AAH IRB considers relevant to the conduct of study.

- sending timely notices to the FDA, OHRP or other agencies as required by regulation and AAH RSPP SOPs with regard to (i) unanticipated problems involving risks to subjects or others; (ii) serious or continuing noncompliance with FDA or HHS regulations, as applicable, or the requirements or determinations of AAH; and (iii) any suspension or termination of IRB approval.

- promptly notify the Relying Institution of the following actions:

  (i) suspension or termination of approval;

  (ii) reports of unanticipated problems or noncompliance;

  (iii) When regulatory agencies and sponsors of relevant IRB actions have been notified of the above actions.

- to the best of their ability, ensure that investigators at external sites conduct the study as approved and in accordance with AAH RSPP SOPS and AAH system policies pertaining to the conduct of human subject research.

  (i) The AAH RSPP provides their SOPs on the [RSPP website](#) accessible by external entities.
(ii) The AAH RSPP delegates this responsibility to the AAH (Lead) research team, who are expected to inform the external sites of the AAH policies and RSPP SOPs pertaining to human subject research.

- act as the HIPAA Privacy Board for Research for the external site when requested. In cases where the authorization is combined with the informed consent document, the research authorization language will be approved as part of the Change to add the external site to the study. HIPAA waiver and alteration determinations will be provided to the external site investigators. [see more below]

- Review identified conflicts of interest and proposed management plans as provided by the external relying institution. The AAH IRB has the right to add to but not remove any elements of the COI management plan created by the external institution.

- dictates the content and format of informed consent document with the exception of site-specific information (e.g., availability of treatment and compensation for research-related injury, payment or reimbursement of research costs incurred by subjects, and local contacts) included in the Local Considerations worksheet - Institution document provided by the external site.

What about HIPAA when AAH is serving as the IRB of Record?

Unless otherwise requested by the relying institution, the AAH IRB will serve as the Privacy Board for the research study. This means that the AAH IRB will make HIPAA waiver and alteration determinations as needed or review and approve required HIPAA authorization language included in the combined consent/authorization document.

The RSPP will provide Privacy Board determinations to the AAH PI/research team, who will in turn provide these determinations to the external research team. It will be the responsibility of the external research team to provide this documentation to the Relying Institution, and to follow their own institution’s policies with regard to executing and storing the research authorization, use and disclosure of subject’s PHI, and accounting of disclosures pursuant to a HIPAA waiver of authorization.

If the AAH IRB is not serving as the Privacy Board for the research study, it is expected that a stand-alone authorization will be used by the Relying Institution to obtain subject authorization for use of his/her PHI for purposes of the research. The AAH IRB will not review the authorization language included in a stand-alone authorization document.

External (Relying) Institution’s Responsibilities

The Relying Institution:

- Shall ensure its Key research personnel on the study are qualified by training and experience pursuant to the Relying Institution’s requirements. This includes monitoring for the need for recertification of HSR training. Failure of key personnel to have appropriate human subject training would be an instance of noncompliance that would be reportable to the AAH IRB.
• Shall ensure its key research personnel on the study are current in their significant financial interest disclosure and COI determinations pursuant to the Relying Institution’s policy.
  
  • Any COI management plan from the Relying Institution must be promptly provided to the AAH IRB for execution. The Relying Institution will be responsible for monitoring the proper execution of COI Management plan. Failure of key personnel to be current with their institutional requirements would be an instance of noncompliance reportable to the AAH IRB.

• Shall ensure that institutional conflicts of interest have been addressed by the Relying Institution per institutional policy.
  
  • The Relying Institution’s COI management plan must be promptly provided to the AAH IRB. Failure to disclose a potential institutional conflict of interest would be an instance of noncompliance reportable to the AAH IRB.

• Will advise appropriate federal agencies, or other relevant parties, as applicable, that AAH IRB is the IRB of record for the research study.

• Shall cooperate and enforce cooperation by their research investigators in providing the AAH IRB any and all information requested by the IRB in a timely manner. This includes, but is not restricted to:
  
  • Information required of the AAH Lead research team for continuing review;
  
  • Current or changes to local context information included in the AAH Local Considerations Worksheet-Institution;
  
  • Any incident that comes that meets the definition of AAH RSPP SOP #7 as a reportable unanticipated problem (UP). The timeframe for reporting these events is noted in the SOP.
  
  • Any incident that meets the definition of AAH RSPP SOP #5 as reportable noncompliance. The timeframe for reporting these events is noted in the SOP.
  
  • Any subject complaint arising from the Research;

• Ensure its own and its investigators’ compliance with AAH IRB’s determinations, with the terms of federal regulations (45 CFR 46) for human subject research and with any other applicable legal requirements or institutional policies and accreditation standards if applicable;

• Shall allow IRB of Record reasonable access to relevant Research records for the purposes of IRB oversight activities or investigations of noncompliance;

• Shall promptly report any changes in the Research conducted at the relying site (including need for immediate temporary or permanent study closure at the site), and not initiate changes in the Research without prior review and approval by the AAH IRB;

• Will not enroll individuals in the Research prior to review and approval by the AAH IRB;
• Shall obtain, document and maintain records of consent and authorization (as applicable) for research subjects.

What are responsibilities of the AAH research team when taking a lead role in the multisite research study?
When AAH IRB agrees to be the IRB of record for external sites in a multisite research study, the AAH research team becomes the Lead Site/research team for the study.

At a minimum, the AAH (Lead) research team is responsible for the following:
• Creating a communication plan to ensure that external study teams are informed of/provided appropriate information about the research study and the AAH IRB decisions. A description of this plan will be requested by the AAH IRB in consideration of acting as an IRB of record for external research sites.
• Directing/coordinating the submission of all materials to the AAH IRB on behalf of each external site.
• Creating a management plan that ensures study subjects are provided with information relevant to their protection or willingness to begin/continue with research participation. This may include: notification of unanticipated problems or instances of noncompliance, provision of significant new information, reconsenting of currently enrolled research subjects with protocol/consent revisions. General information on the plan to provide information to research subjects will be included in the site’s submission of this information to the AAH IRB. However, the Lead site is responsible for ensuring that the external sites follow the requirements of IRB approval.
• Informing all external sites/individuals that they **MUST** follow AAH RSPP SOPs and guidance documents in the conduct of the research;
• Collecting information from external sites related to subject accrual and withdrawal, UPIRSOs, noncompliance, subject experiences, etc, and recording on continuing reivew form submitted to the AAH IRB as applicable.

Additional guidance on the responsibilities involved in serving as a lead research site may be found on the SMART IRB website: **Overall Principal Investigator/Lead Study Team Guidance and Checklist** (part of the Study Team package located at [https://smartirb.org/study-teams/](https://smartirb.org/study-teams/)). The information provides a checklist that study teams may find useful in taking on Lead study team responsibilities.

**REQUIREMENTS**
• Common Rule Regulations: 45 CFR 46.114
• OHRP guidance: **Single IRB Exception Determinations**
- AAHRPP Accreditation Standards/Elements: I.9
- AAH System Policy: 2467
- AAH RSPP SOPs: SOP 1, 2, 9