GUIDANCE DOCUMENT ON THE DEFERRAL/CEDING OF AURORA IRB OVERSIGHT TO AN EXTERNAL IRB

Aurora Health Care’s Research Subject Protection Program (RSPP)

This guidance serves to address DHHS (45 CFR 46.108, 45 CFR 46.114) and FDA expectations (21 CFR 56.108, 56.114) with regard to an institution’s reliance on an external IRB. If not defined herein, see Glossary for definition of terms.

In accordance with the Aurora RSPP Statement of Authority and Purpose, all human subject research conducted at Aurora must be either reviewed by the Aurora 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 which allows an institution holding a Federal Wide Assurance (FWA) to defer IRB review to a second FWA-holding institution.

Note that the decision to defer Aurora 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.

To Which External IRBs will the Aurora IRB Defer

The determination to defer IRB oversight to an external IRB is a decision made solely by the Aurora RSPP. A Request to Rely on an External IRB must be submitted to the Aurora RSPP Central IRB office (centralirb.office@aurora.org) to begin this consideration. To be eligible for external IRB review, a study must have administrative approval from Aurora Research Institute (Research Administration Pre-authorization process), and meet one of the criteria noted in SOP 409, section 1.1.

Studies not meeting the ceding criteria will be given individual consideration by the RSPP Director, in consultation with the Institutional Official as necessary (SOP 409, 1.1.5).

The human research protections program (HRPP) of Aurora Health Care must adhere to the standards set by AAHRPP (Association for Accreditation of Human Research Protection Programs) for accreditation. In deciding whether the Aurora IRB will defer oversight to an external IRB, the Aurora IRB takes into account whether the external IRB is 1) AAHRPP-accredited or 2) has an HRPP that is comparable to AAHRPP standards. To determine the latter, the Aurora RSPP Director (or designee) will review the external IRB’s policies and procedures to ensure they are equivalent those of an AAHRPP accredited institution. A checklist provided by AAHRPP may be used in this consideration. If the proposed IRB of Record does not meet these standards, it is unlikely the Aurora IRB will consider ceding IRB oversight to that institution.

If the Aurora RSPP determines that deferral of the study to an external IRB is not warranted, the research study must be submitted in accordance with Aurora RSPP SOP 301.
IRB Reliance Agreements

Once the decision to defer has been made by the Aurora RSPP, an IRB Reliance Agreement (IRA) must be executed unless one already exists.

- An IRA may be executed between two institutions or a group of institutions.
- An IRA may require extended discussions between institutions and involve consultation with legal counsel.
- IRA should identify any apportionment of IRB review responsibilities.
- IRA 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.
- IRA clearly communicates 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.
- IRA communicates plan 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.
- IRA 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.
- A copy of the IRA signed by both institutional officials must 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 research to which the FWA applies.

The Aurora RSPP has a template IRA available that takes into account these points. It is our preference that the Aurora template be used as it has been vetted by Aurora legal counsel. If another document is used, time will be needed for legal counsel review of this document.

What Happens Upon Deferral of Aurora IRB Oversight...

Once the IRA has been signed by all required parties, the Aurora PI will receive notification of deferral from the Aurora IRB as well a copy of the IRA.

- Upon deferral of Aurora IRB oversight and the approval of the study by the external IRB, the external IRB becomes the IRB of Record for that study. The Aurora PI 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.
• The Aurora PI may NOT begin that research project until approval has been received from the IRB of Record. This includes the recruitment of subjects.

• Per Aurora RSPP SOP 409, the Aurora PI must notify the Aurora IRB when reports are made to the IRB of Record of local potential unanticipated problems, instances of serious or continuing non-compliance, and suspension or termination of the research.

Note that:

• Studies deferred to an external IRB may be included in the standard audit sample;

• Aurora Leadership (administrators, Institutional Official, Senior Vice President of Research) may review and approve/disapprove the conduct of any research study at Aurora Health Care, but these individuals may not approve the conduct of the research if it has not been approved by the external IRB.

RESPONSIBILITIES OF PARTIES IN THE DEFERRAL PROCESS

1. Responsibilities of the **Aurora Principal Investigator (PI)** include, but are not limited to:

   • Agree to follow Aurora RSPP SOP 409.

   • Acknowledge that Significant Financial Interests of all study key personnel must be reported per Aurora Policy 269 and Aurora RSPP SOP 104.

   • Acknowledge that active status in Aurora Research Certification is to be maintained for all study key personnel.

   • Comply with the external IRB’s policies, directives and determinations.

   • Provide the external IRB with any requested information about local context, resources and/or personnel at the research sites.

   • Agree to provide Aurora RSPP contact information to the external IRB for future correspondence.

   • Agree to cooperate with the external IRB with regard to initial and continuing review, record keeping and reporting. All information requested by the IRB must be provided in a timely manner.

   • Agree that enrollment of subjects may not occur until study approval is granted by the external IRB.

   • Promptly to the external IRB any proposed changes in the research (including key personnel changes) as directed by the external IRB’s SOPs.

   • Will not initiate changes in the research (including changes in the consent document) without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the participants.
• Acknowledge that the study team 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.

• Ensure 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 external IRB of any study specific incidence, experience, or outcome that rises to the level of an unanticipated problem and/or serious or continuing non-compliance.

• Obtain, document, and maintain records of consent for each subject or subject’s legally authorized representative as stipulated by the external IRB (as necessary per the study approval).

• Maintain appropriate study records.

2. **Aurora Health Care/Aurora IRB** responsibilities include, but are not limited to:

   • Prior to deferral agreement, verify COI and Research Certification status for all study key personnel.

   • Make appropriate and necessary HIPAA determinations.

   • Execute IRB Reliance Agreement, if necessary/applicable.

   • Comply with the external IRB’s requirements and directives.

   • Provide the external IRB with any state, local, or institutional requirements with regard to the protection of human subjects.

   • Acknowledge that Aurora Health Care 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.

   • Ensure the safe and appropriate performance of the research at Aurora Health Care. This includes but is not limited to:

     o Monitoring ongoing research certification and potential conflict of interest of key study personnel;

     o Monitoring protocol compliance;

     o Maintaining compliance with state, local, or institutional requirements related to the protection of human subjects;

     o 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 external IRB of any 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 external IRB.

- With regard to inclusion of adults with impaired decision making capacity, provides the external IRB with details regarding state law and institutional policy relative to the authority of legal guardians to consent to research.

3. **External IRB** Responsibilities include, but are not limited to:

- 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 Aurora IRB 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 the Aurora IRB, 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 relying institution.

- Make available to the Aurora Health Care 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 Aurora Health Care) of its determinations and decisions.

- When appropriate, conduct on-site or remote post-approval monitoring or audits, unless delegated to Aurora Health Care.
• Promptly notify Aurora Health Care if there is a suspension or termination of the external IRB’s approval of the study or the external IRB’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.

Resources


AAHRPP Tip Sheet: Relying on An External IRB