Aurora Research Subject Protection Program (RSPP)
Guidance Document

Conducting Investigator-Initiated Multisite Collaborative Research Activities

The purpose of this guidance document is:

- to describe considerations and expectations for investigator-initiated research (research not sponsored by industry or an established cooperative group such as GOG, ECOG, etc.) that involves multiple sites and Aurora is the coordinating center;
- to describe the expectations for data management when a principal investigator from Aurora is lead investigator, or when Aurora is considered the Coordinating Center;
- to help the protocol development process and avoid delays and additional questions during IRB review.

Please call the RSPP office at 414.219.7744 with any questions.

What is multisite research?

"Multisite" research refers to research that will be conducted at both Aurora *and* non-Aurora locations. There are several possible scenarios to which this guidance applies:

- An investigator-initiated clinical trial to be carried out by investigators at more than one institution and Aurora is the coordinating center.
- A protocol where the Aurora investigator is conducting research at one or more sites not under the control of Aurora (for example, schools, nursing homes, other healthcare facilities, etc.).
- An Aurora investigator is conducting interventions with subjects at Aurora and sharing identifiable data collected for that study with researchers at another university or institution.
- An Aurora investigator is receiving identifiable data or specimens collected from non-Aurora sites to be analyzed for the purpose of answering a research question.

Multisite studies do NOT include:

- Studies involving multiple Aurora locations that fall under the purview of the Aurora IRB. For example, a study conducted at both Aurora St. Luke's and Aurora BayCare is NOT considered multisite research.
- Multicenter clinical trials conducted by an industry sponsor or an established cooperative group.

What is a Coordinating Center?

A Coordinating Center is responsible for overall data management, monitoring and communication among all sites, and general oversight of study conduct. Responsibilities associated with serving in the capacity of a coordinating center will depend on the type of research and level of risk to subjects, and include one or more of the following:

- Designing and developing the protocol and template informed consent documents for use at each collaborating institution
- Selecting appropriately qualified study sites/principal investigators
- Obtaining documentation of IRB approval from each collaborating institution prior to enrollment of subjects at that site, or obtaining an appropriate IRB reliance agreement
- Maintaining documentation of all external sites' initial and continued IRB approval for the protocol

- Ensuring, if the study is PHS (federally) funded, that each collaborating institution holds an applicable OHRP-approved Federal Wide Assurance (FWA)
- Collecting and maintaining critical documents from external investigators indicating their qualifications and training germane to their research activities and according to their site's requirements (e.g. resume/CV, medical license, certification of completion of human subject protection or other required training, laboratory certifications and laboratory norms , appropriate conflict of interest disclosures, administrative approvals)
- Storing and/or managing study-wide data, data analysis, and ensuring appropriate data and safety monitoring
- Protecting the confidentiality of data
- Ensuring informed consent is obtained and documented from each subject in compliance with federal regulations and IRB approval
- Providing study specific training to the research personnel at the external sites
- Developing and providing protocol-specific case report forms for each external site
- Coordinating randomization as applicable
- Registering subjects and tracking subject enrollment
- Ensuring that external sites are using the correct version of the protocol and consent document
- Tracking, reporting and maintaining documentation of all serious adverse events and unanticipated problems, and disseminating the information to external sites in a timely manner
- Providing periodic updates to external investigators on subject enrollment, general study progress, and relevant scientific advances and significant new findings
- Assuring that all relevant IRB correspondence (continuing review, amendments, significant new findings) and study status changes are communicated to all external sites
- Documenting receipt, shipment and storage of study specimens, drugs and/or devices
- Periodic monitoring at the non-Aurora sites to assess research study progress and compliance with the IRB approved protocol
- Securing compliance at non-Aurora sites that are not adhering to the current version of the research protocol and/or good clinical research practices
- Terminating the involvement, if necessary, of noncompliant investigators and reporting such action to the appropriate IRB

The roles and responsibilities of each site must be understood and outlined in a separate agreement or the approved protocol.

The Aurora IRB must understand Aurora's and the Aurora investigator's role in these activities. When the Aurora IRB will be the IRB of record for such activities, the IRB will need assurances that adequate resources and expertise to carry out these additional responsibilities are available.

What are Aurora IRB requirements for multisite collaborative research studies?

Although multisite studies undergo the same type of IRB review as single site studies, the specific IRB review will depend upon Aurora's role in the multisite research. The IRB will need to determine whether non-Aurora sites or non-Aurora personnel need IRB approval in order to participate in the study activities. In addition, the Aurora IRB requires that all multisite research studies have a protocol, regardless of the study's risk level. The Aurora RSPP/IRB website has protocol templates available.

When Aurora is the lead site, study-wide information (such as accrual and withdrawal numbers, unanticipated problems, subject experiences) will need to be reported to the Aurora IRB at Continuing Review in addition to site-specific information.

When is IRB approval required for an external site or personnel?

Whether IRB approval is required depends on whether the non-Aurora site or non-Aurora personnel are engaged in human subject research as defined by federal guidance (http://www.hhs.gov/ohrp/policy/engage08.html). It also can depend on whether a study qualifies for an exemption. Determining whether a non-Aurora site or non-Aurora personnel are engaged in research can be difficult. Researchers are encouraged to consult with the RSPP Director (414.219.7740) for guidance early in the protocol development process.

Will the Aurora IRB consider serving as the IRB for a non-Aurora site or personnel?

Yes. Depending on the nature of the study and the activities that will be conducted by the non-Aurora sites or non-Aurora personnel, the Aurora IRB may consider serving as their IRB of record. **Check with the individual site's IRB first as that may not be consistent with their policies.** Anyone for whom the Aurora IRB serves as IRB of record must be listed as investigator/key personnel and must complete Aurora's human subject research training and conflict of interest disclosures.

Will the Aurora IRB consider ceding IRB oversight to another IRB?

Yes, in limited circumstances, although it depends on the nature of the study and the study activities to be conducted at Aurora. Please contact the RSPP Director early in the discussion phase and prior to any submission to the Aurora IRB if you would like to make such a request.

Does the Aurora IRB have any agreements with other IRBs regarding oversight of multisite studies?

Yes, the Aurora IRB has the following agreements in place that may assist researchers in conducting multisite and collaborative research:

- Wisconsin IRB Consortium (WIC) agreement, which also includes Marshfield Clinic, Medical College of Wisconsin and University of Wisconsin Madison. WIC allows for eligible studies involving multiple WIC institutions to potentially be reviewed by a single IRB of record. Please visit www.wicshare.com for details or call the RSPP Director or RSPP Supervisor with questions.
- Agreement with the NCI CIRB for review of certain phase III adult oncology studies.
- Agreement with the University of Wisconsin – Milwaukee IRB for certain types of activities being conducted by UWM students or faculty.
- The Aurora and Marquette University IRBs have an agreement to consider ceding of IRB oversight responsibilities on a case-by-case basis.

Does the IRB review process take longer for multisite studies?

Depending on the complexity of the study and the quality of the application and study protocol, the IRB review process may take additional time. Coordinating IRB reviews for other sites and/or preparing agreements for the Aurora IRB to serve as IRB of record for non-Aurora sites or personnel can take additional time as well. A well-prepared application and study protocol can help to ensure that the IRB review process goes as smoothly as possible. Staff in the RSPP as well as Investigator-Initiated Research of the Aurora Research Institute are available for consultation at any time during the protocol development phase.

Additional considerations

- Prior to submitting any research proposal to the Aurora IRB, the Aurora investigator must obtain Research Administrative. This administrative clearance may be obtained by submitting an email to the RAP inbox (research.preauthorization@aurora.org) Confirmation of research administrative clearance for the project MUST be included with the submission to the Aurora IRB. The IRB submission will be considered "incomplete" until this document is provided to the Aurora RSPP/IRB office.
- A contract or data/material transfer agreement may be required. This will be considered during the administrative review process.
- IRB fees for review may apply.
