

<b>SOP: Number OI 1101</b> <b>Version No: 04</b> <b>Effective Date: 07/01/08</b>	<b>LOCAL FACILITATED REVIEW</b> <b>OF NCI CIRB APPROVED</b> <b>PROTOCOLS</b>	<b>Supersedes</b> <b>Document Dated:</b> <b>01/22/07</b>
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## 1. POLICY

This policy outlines the mechanism by which the Aurora IRB can conduct a facilitated review to accept approval and ongoing-oversight of the National Cancer Institute’s (NCI) Central Institutional Review Board (CIRB) in lieu of full board review by the Aurora IRB. Authority is granted through an executed IRB Authorization Agreement between Aurora IRB and NCI CIRB. This policy also outlines procedures for submitting to the Aurora IRB related to NCI CIRB approved protocols.

The CIRB Initiative is a pilot project sponsored by the NCI, in collaboration with the DHHS Office for Human Research Protections (OHRP), to develop an innovative approach to human subjects protection for national multi-center cancer trials. The NCI CIRB provides review of Phase 3 Cooperative Group adult cancer treatment protocols and selected other cancer trials. Following review by the CIRB, and upon submission of required documents by the local investigator (as outlined in this policy), the Aurora IRB downloads documentation from the CIRB website and the IRB Chairperson, or designated reviewer, performs a facilitated review of the CIRB’s review of a particular protocol. If the CIRB’s review is determined to be acceptable and there are no concerns about the local research context, the IRB Chairperson, or designated reviewer in consultation with the IRB Chairperson, can decide to accept the CIRB review of the particular protocol, in lieu of a full board review by the Aurora IRB. The CIRB becomes the IRB of record for the particular study and performs all future continuing reviews, amendment reviews, and reviews of non-local serious adverse events for the life of the study. The IRB Chairperson, or designated reviewer in consultation with the IRB Chairperson, retains the option of not accepting the CIRB review and may choose to defer for full board review by the Aurora IRB.

It is understood that the CIRB’s primary function is initial and continuing review of protocols, and the primary function of the Aurora IRB is consideration of local context and oversight of local performance for these protocols, as outlined below.

### Specific Policies

#### 1.1. The Responsibilities of the NCI CIRB are to:

1.1.1. Perform initial reviews of new protocols, discuss any issues with the sponsoring Group and Study Chair, and make a final decision of approval or disapproval of the protocol according to all criteria established by federal regulations;

1.1.2. Maintain and make accessible to the Aurora IRB the CIRB application, protocol, informed consent, primary reviews, minutes, notification letters, and correspondence from Groups;

1.1.3. Carry out Continuing Reviews, reviews of non-local Serious Adverse Events, reviews of protocol amendments, reviews of DSMB reports, and reviews of any other documents submitted by the sponsoring Group or Study Chair;

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1.1.4. Notify the Aurora IRB of any new materials that have been reviewed for an active protocol and any changes in the protocol approval status;

1.1.5. Maintain an OHRP-approved Assurance for human subjects research;

1.1.6. Maintain a Board membership that satisfies the requirements of 45 CFR 46 and provide special expertise as needed from Board members or consultants to adequately assess all aspects of each protocol;

1.1.7. Make available to the Aurora IRB the roster of CIRB membership and the CIRB Standard Operating Procedures and policies;

1.1.8. Ensure that CIRB members receive proper initial and continuing education on topics relevant to human subjects protections;

1.1.9. Notify the Aurora IRB immediately if there is ever a suspension or restriction of the CIRB's authorization to review protocols; and

1.1.10. Notify the Aurora IRB of any CIRB policy decisions or regulatory matters that might affect the Aurora IRB's reliance on CIRB reviews or performance of the research at Aurora Health Care.

**1.2. The responsibilities of the Aurora IRB are to:**

1.2.1. Ensure the safe and appropriate performance of the research at Aurora Health Care. This includes, but is not limited to, monitoring protocol compliance, protocol violations and serious adverse events occurring at the institution, and providing a mechanism by which complaints about the research can be made by local study participants or others. Any actions taken as a result of problems that are identified in these areas will be shared with the CIRB and reported as required by the procedures established by the protocol's sponsoring Group;

1.2.2. Ensure that the investigators and other staff at Aurora Health Care who are conducting the protocol are appropriately qualified and meet the institution's standards for eligibility to conduct research;

1.2.3. Provide to the CIRB and keep current the names and addresses of contact persons who have authority to communicate for the Aurora IRB, such as the Manager of the RSPP;

1.2.4. Establish a procedure by which the Aurora IRB will receive and review the CIRB materials for protocols to be performed at Aurora Health Care. For each CIRB reviewed protocol (approval or disapproval) that is submitted to the Aurora IRB by a local investigator, the Aurora IRB shall:

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- Review the CIRB’s materials;
- Determine if there are any local context issues that must be addressed by the local IRB; and
- Decide whether to accept the CIRB review or conduct a separate local review by the Aurora IRB.

1.2.5. Review local adverse events on CIRB approved protocol in accordance with Aurora IRB policy RR 403. If it is determined that the reported event is or may be an unanticipated problem involving risks to subjects or others, the local PI will be instructed to report the event to the NCI cooperative group who in turn will report to NCI CIRB.

1.2.6. Report to the CIRB the decision about local acceptance/rejection of the CIRB review. Notify the CIRB if there is ever a change in the acceptance/rejection of the CIRB review;

1.2.7. As appropriate, add local restrictions, stipulations, or substitutions to CIRB approved informed consents. Deletion of CIRB approved requirements in the protocol and Informed Consent Form is not allowed, and substantive changes that affect the meaning of CIRB approved requirements are not allowed;

1.2.8. If the Aurora IRB accepts the CIRB approval of a protocol, maintain documentation of the decision and evidence that it has received and considered all CIRB material relevant to the protocol;

1.2.9. Maintain an OHRP approved Assurance for human subjects research;

1.2.10. Maintain an IRB whose membership satisfies the requirements of 45 CFR 46;

1.2.11. Maintain a human subjects protection program, as required by the DHHS OHRP;

1.2.12. Ensure that the Aurora IRB members and local investigators receive proper initial and continuing education on the requirements related to human subjects protections;

1.2.13. Notify the CIRB immediately if there is ever a suspension or restriction of the Aurora IRB’s authorization to review protocols; and

1.2.14. Maintain compliance with any additional state, local, or institutional requirements related to the protection of human subjects.

### **1.3. Procedure**

1.3.1. Aurora Health Care investigators wishing to open a CIRB-approved protocol must submit the following to the Aurora Research Subject Protection Program (RSPP):

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- A completed Aurora NCI CIRB Protocol Submission Application for Facilitated Review (form OI 1101-A)
- CIRB Application from the “Participant’s Area” of the NCI CIRB website ([www.ncicirb.org](http://www.ncicirb.org));
- The complete protocol from the NCI CIRB website (including any amendments not incorporated into the full protocol);
- A copy of the current Investigator’s Brochure for any investigational agents or the package insert for approved drugs to be used in the research. The Investigator’s Brochure must be obtained by contacting the cooperative group sponsoring the research;
- Informed consent document(s) from the NCI CIRB website, incorporating Aurora IRB’s recommended template language (see form IC 701-A), including HIPAA authorization, and formatting (e.g., Aurora consent form headers and footers, consent form section headings, required template language concerning research-related injury, local contact information, signature section, etc.);
- Copies of any surveys and/or questionnaires to be used in the research, and any diary cards or other study related information that will be provided to subjects (medication instructions, etc.). These are generally available on the NCI CIRB website;
- Any site-specific documents, such as recruitment materials and all other materials to be seen by subjects;
- Other required documentation for investigators conducting research at Aurora facilities (see SOP FO 301, section 1.1.2 for detailed information).

1.3.2. Upon receipt of the above-noted submission materials, RSPP staff verifies that the principal and co-investigators have completed the necessary human subject protection training and that credentialing verification letters are on file. RSPP staff will download the following documentation from the “Participant’s Area” of the CIRB website:

- Minutes detailing the CIRB’s review of the protocol;
- CIRB primary reviewers’ (scientific and non-scientific) reviews;
- Last continuing review documentation (including reviewer’s notes), if applicable;
- Summary of adverse event reports;

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- Related correspondence, including requests for changes and or modifications, and final approval notices;
- Any other relevant information that may affect the IRB Chair, or designated reviewer’s, decision to accept the CIRB review of the protocol.

This material along with all material submitted by the local investigator is forwarded to the IRB Chair or a “designated reviewer” (any other IRB member designated by the IRB Chair at the time of submission).

1.3.3. The IRB Chair, or designated reviewer, conducts a facilitated review. The purpose of the facilitated review is to determine whether there are local concerns that need to be addressed and whether to accept the CIRB review. There are three possible outcomes of this facilitated review:

- Deferred to the Aurora IRB (Protocol Not Accepted): Oversight by the Aurora IRB is required for this protocol. The investigator will be required to prepare a full submission (see SOP FO 301) to be considered by the convened IRB at a future meeting. The CIRB will not be involved in overseeing the protocol.
- Minor Modifications Required: Specific stipulations must be addressed before the CIRB can be designated as the IRB of record. See 1.3.4 below.
- Accepted: The Aurora IRB accepts the review of the CIRB. The CIRB will be designated as the IRB of record.

1.3.4. As part of the facilitated review, the IRB Chair, or designated reviewer, may add stipulations or local requirements to protocols, particularly to increase subject safety, to clarify procedures, etc., but may not delete or contradict any protocol contents. Local boilerplate additions or deletions to the informed consent, dealing with state and local law, institutional requirements, or IRB policies, may be appropriate. The IRB Chair, or designated reviewer, may also make minor word substitutions or additions in the informed consent document, particularly to facilitate better comprehension by the local population, as long as the proposed changes do not alter the meaning of the CIRB approved consents. As with other cooperative group protocols, the local research study staff will be responsible for sharing informed consent changes with the appropriate cooperative group.

1.3.5. Aurora RSP staff will notify the CIRB Administrative Office each time the IRB Chair, or designated reviewer, accepts the CIRB review of a protocol. This is done by clicking on the “Facilitated Review Acceptance form” button/link on the CIRB website (within the main menu for each protocol) and following the directions for completing the “Facilitated Review Acceptance Form.”

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1.3.6. RSPP Manager will notify the PI in writing each time the Aurora IRB accepts the CIRB review of a protocol.

1.3.7. RSPP Manager will complete the CTSU IRB Certification Form, if applicable. This form will be provided to the PI for submission to CTSU to document the Aurora IRB’s acceptance of review by the CIRB.

1.3.8. The Full IRB will be notified of the acceptance of CIRB review via a list to be included as part of each month’s IRB agenda and minutes. The list will include studies open at Aurora Health Care that received a facilitated review. Any IRB member may request access to the materials reviewed as part of the facilitated review. A majority of members of the IRB must vote to require full board review of any protocol previously reviewed and approved under the facilitated review process.

1.3.9. If the IRB Chair, or designated reviewer, accepts CIRB review, they also allow continuing review by CIRB. Continuing review by CIRB includes review of at least annual progress reports, study-wide adverse events, amendments, study-wide recruitment materials, etc. During the course of the study, local adverse events and site-specific needs (e.g., any changes in current recruitment methods or mechanisms, changes in local research site personnel, changes in locations where the research is being conducted, and local investigator-initiated consent form changes) must be submitted by the local investigator according to Aurora IRB policy RR 403. These local adverse events and site-specific items will be reviewed under the Aurora IRB’s Full Board or Expedited procedures as deemed appropriate by RSPP staff and IRB Chair.

- At least annually, the local investigator will be required to complete and submit to the Aurora RSPP a Progress Report / Study Closure Notice for NCI CIRB Protocol (form OI 1101-D). Upon receipt of the completed form, RSPP staff will download NCI’s continuing review report. Study materials (both study-wide and local) will be reviewed to determine if the study was amended in any way by the NCI CIRB, or if modifications are needed to the local consent document. Local information will also be reviewed for compliance with Aurora IRB policies. Study materials will be reviewed by the IRB Chairperson or designated reviewer. The IRB Chair or designated reviewer will document continued acceptance of CIRB oversight of the study by signing this form.
- Aurora RSPP staff will be notified by CIRB when additional reviews are conducted and will follow the steps outlined under 1.3.10 below. The RSPP Manager will complete a CTSU IRB Certification Form at the time of continuing review, if applicable. This form will be provided to the local investigator for submission to CTSU to document the Aurora IRB’s continued acceptance of review by the CIRB.

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1.3.10. Upon receipt of e-mail notification by CIRB of additional material reviewed, RSPP staff will retrieve the associated documentation from the CIRB website and forward the notification and documentation to the IRB Chair, or designated reviewer, who will review and sign each document to acknowledge that it has been considered. The purpose of this review is to ensure that any additional local concerns are addressed and consent form modifications are made when appropriate. Any local revisions to the consent form initiated by the Cooperative Group, or mandated by the CIRB, should be submitted to the Aurora IRB according to policy RR 403. Other consent form changes, within the scope of those changes described under 1.3.4 of the procedure section of this policy, must be approved by the IRB Chair. The IRB Chair, the designated reviewer, or Aurora RSPP staff may also ask local investigators to provide additional information related to any item being reviewed, as needed. Anytime changes are made to the IRB approved consent form, Aurora IRB staff will provide the local investigator with a copy of the current approved version of the consent form to be used. The RSPP Manager will complete a CTSU IRB Certification Form at the time of CIRB approval of certain protocol amendments (as required by CTSU). This form will be provided to the local investigator for submission to CTSU to document the Aurora IRB's continued acceptance of review by the CIRB.

1.3.11. Any local changes to CIRB reviewed protocols (e.g., the addition of a new investigator or study site, new or revised recruitment materials, additional subject information, etc.) must be submitted to the Aurora IRB as outlined in SOP RR 403 (section 1.3) for review prior to implementation of the change. The appropriate form should be accompanied by any supporting documentation (e.g., investigator Conflict of Interest statements, etc.) required by the change. Such requested changes will be reviewed for completeness by the Aurora RSPP staff and approved by the IRB Chair, or designated reviewer. Approval of the requested change(s) will be communicated to the investigator or study coordinator. Revised Investigator Brochures should be submitted to the Aurora IRB as outlined in SOP RR 403 (section 1.5) when the investigator/study staff becomes aware of any revisions/additions to this document.

1.3.12. The Aurora IRB remains responsible for the review of local protocol violations and adverse events, including local deaths. The Principal Investigator must report local events occurring on CIRB reviewed protocols to the Aurora IRB. Local adverse event reporting will follow the procedure outlined in Aurora IRB SOP RR 403 and will be reported using the appropriate form (Form RR 403-A). Local protocol violation reporting will follow the procedures outlined in Aurora IRB SOP RR 403 and will be reported using the appropriate form (RR 403-G).

1.3.13. At the time of study closure, the local Principal Investigator will be required to submit a completed Progress Note / Study Closure Notice for NCI CIRB Protocol (Form OI 1101-D) that will be reviewed for completeness by RSPP staff, and if determined necessary, will be forwarded to the IRB Chair, or designated reviewer, for review.

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1.3.14. All CIRB and local material reviewed by the IRB Chair, or designated reviewer, and documentation of the decision to accept or reject CIRB review will be retained in a protocol file as dictated by the Aurora IRB's record retention policy (see Aurora IRB SOP FO 305).

1.3.15. CIRB reviewed protocols will be included in the pool of studies eligible for internal audit. Internal audit will focus on verification that procedures noted in this policy were followed.

1.3.16. Additionally, the RSPP Manager will notify the CIRB Administrator of actions taken as a result of problems identified in the areas of protocol compliance, protocol violations, serious adverse events, and complaints from subjects; provide to the CIRB and keep current the names and addresses of local contact persons who have authority to communicate for the local IRB; and notify the CIRB immediately if there is ever a suspension or restriction of the local IRB's authorization to review protocols.

## **2. SCOPE**

These policies and procedures apply to all NCI protocols submitted for CIRB designation (phase III, adult, cooperative oncology group studies).

## **3. APPLICABLE REGULATIONS AND GUIDELINES**

FDA Guidance for Industry: Using a Centralized IRB Review Process in Multicenter Clinical Trials March 2006

## **4. REFERENCES TO OTHER APPLICABLE SOPS**

SOP FO 301

SOP FO 305

SOP RR 403

SOP IC 701