



Division of Responsibilities between the Central IRB and Enrolled Local Institutions

The following Division of Responsibilities is based on the premise that the NCI Central IRB's (CIRB) primary function is IRB review of adult and pediatric Cooperative Group research studies and that the local institution's primary function is consideration of local context and oversight of local performance of these studies. The local institution, through its own local IRB, decides on a study-by-study basis whether to accept the CIRB's review for a particular study or to conduct its own local IRB full Board review.

The responsibilities of the CIRB are to:

- 1) Perform initial full Board review of new studies, discuss any issues with the Cooperative Group Study Chair, require modifications to be made by the Study Chair, and make a final decision of approval or disapproval of the study;
- 2) Conduct Continuing Review;
- 3) Conduct review of study amendments;
- 4) Conduct review of individual Adverse Event Reports for studies without a Data and Safety Monitoring Board (DSMB), such as most Pilot and Phase 2 studies;
 - a) Individual Adverse Event Reports distributed by the Cooperative Groups for studies which have a DSMB do not receive CIRB review. The CIRB reviews the DSMB report and the study report at the time of continuing review as recommended in the following Guidances: OHRP Guidance "OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events" dated January 15, 2007, FDA Guidance "Adverse Event Reporting to IRBs – Improving Human Subject Protection" dated January 2009, and NIH Guidance "Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multicenter Clinical Trials" dated June 11, 1999;
- 5) Conduct review of all other documents submitted by the Study Chair;
- 6) Provide the CIRB application, primary reviewer reviews, outcome letters, minutes and other relevant documents to the designated IRB at the local institution;
- 7) Notify each local institution of new materials that have been reviewed for an active study and any changes in the study approval status;
- 8) Maintain a CIRB 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;
- 9) Make available to the local institution the roster of CIRB membership and the CIRB Standard Operating Procedures;
- 10) Ensure that CIRB members receive orientation and continuing education on topics relevant to human subjects protection;
- 11) Notify the local institution immediately if there is ever a suspension or restriction of the CIRB's authorization to review a study; and
- 12) Notify the local institution of any changes in CIRB SOPs that might affect the institution's reliance on CIRB reviews or performance of the research at the local institution.

The responsibilities of the local institution are to:

- 1) Ensure the safe and appropriate performance of the research at its institution. This includes, but is not limited to, monitoring protocol compliance, managing any major protocol violations, managing any serious adverse events occurring at the institution, ensuring qualifications of research staff and providing a mechanism by which complaints about the research can be made by local study participants or others.
- 2) Provide the names and addresses to the CIRB Operations Office of local contact persons who have authority to accept a facilitated review and/or correspond on behalf of the local IRB (e.g. the local IRB Director).
- 3) Establish a written procedure for performing facilitated review.
- 4) Maintain records for each CIRB approved study opened at your institution as per your local institution policy.
- 5) Maintain an OHRP-approved Assurance for human subjects research and an OHRP IRB registration number;
- 6) Maintain a human subjects protection program compliant with 45 CFR 46 and 21 CFR 56; and
- 7) Maintain compliance with state, local, or institutional requirements related to the protection of human subjects.

Further Delineation by Topic (alphabetically)

Assent (for pediatric trials)

The CIRB makes the determination whether assent of the child is required. Whether and how to document assent is the purview of the local institution.

HIPAA

Compliance with HIPAA regulations are considered local context issues and remain the purview of the local institution and local IRB.

Incompetent Adults

The CIRB determines whether ‘individuals with impaired decision making capacity’ as a category are eligible for a study. The local institution must follow state law and institutional policy regarding the authority of legal guardians to consent to research, as well as documentation of proxy consent.

Informed Consent Document

As part of facilitated review, the local IRB chair/subcommittee may

- Add local boilerplate additions to the informed consent document to comply with state or local laws, institutional requirements, or IRB policies
- Make minor word substitutions or additions in the informed consent document to facilitate better comprehension by the local population as long as the proposed changes do not alter the meaning of the CIRB approved contents.

The informed consent text may not be otherwise deleted or contradicted. Revisions/changes to the informed consent document other than those described above require full Board review at the local level, and facilitated review may not be used.

The translation of the informed consent document is the responsibility of the local institution.

Prisoners

The CIRB is not constituted to review studies eligible for prisoners, per 45 CFR 46 Subpart C, so cannot be the IRB responsible for review if the local investigator wants to enroll a prisoner. If the local investigator wants to enroll prisoners on a particular study the local IRB must conduct a full board review of the study as per Federal regulations.

Serious Adverse Events

Serious adverse events that occur at the local institution must be reported to the local IRB as per local institutional policy and should not be reported to the CIRB. The investigator should continue to report SAEs to the Cooperative Group per the study protocol.

Reporting Unanticipated Problems

Local unanticipated problems occur at and are limited to a specific institution. The local institution is responsible for managing these according to its FWA and local institutional procedures. If the local IRB determines that an unexpected incident, event or outcome meets the regulatory definition of unanticipated problem, it is the local institution's responsibility to report it to OHRP/FDA.

Unanticipated problems within the purview of the CIRB are those unexpected incidents, events or outcomes which the sponsor identifies and which impact the trial nationally. These are reviewed by the CIRB and the CIRB accepts the responsibility to ensure reporting to the appropriate agency, i.e. OHRP and/or FDA.