

10/01/03

To: Joal Hill  
Chair, Advocate IRB

From: Bryan Coyle

Re: NCI's Central Institutional Review Board Initiative

The Advocate IRB can participate in the NCI Centralized Review Initiative (CIRB) by amending our current FWA to list their Board as one of our IRBs. The advantages of participation to local investigators and the Board's workload are self-evident. Additionally, the efficiencies offered and the mandatory continuing role of local IRB's in the approval process should improve subject protections. At this time, this central review process is available for adult, phase III trials.

Since the Advocate Board participates in the CIRB, local investigators would submit exactly the same package as proposed in the 'Facilitated Protocol Reviews' memo for studies proposed at a site after they are already open at another site within Advocate. The only difference would be that the initial Full review will have been conducted by the CIRB rather than by our reviewer and local Board. A designee of the Chair would be responsible for the same facilitated review of the site specific materials, including the consent form that should adhere to the Advocate template.

The principal investigator on a new submission submission to Advocate that is already CIRB approved would provide (**2 copies** of):

- standard AHCIRB cover page with all contact information and signature; title and current revision level should be the same as currently open
- fee waiver request or billing information
- institutional signatures as needed (pg 2 of application pack)
- the full sponsor protocol – download and print; no abridged Advocate forms needed other than Page 7 with the anticipated number of patients to be included and any IDE or IND information
- relevant staff listing and ethics credentials, as needed (items XII & XIII)
- required support department resources, if relevant (item XVIII)
- consent form as previously approved with changes only to the site specific information: PI, Co-Investigators, site, contact phone numbers and Advocate template materials
- electronic copy of the consent form to receive a unique IRB number and approval date

Once approved, the protocol would be treated as they are now. The annual review cycle would commence upon approval and be specified to expire at the same time as that of the original protocol. The site PI would be responsible for reporting local SAE's, the periodic review form and sponsor amendments. Presumably, when a single protocol is open at multiple Advocate sites, the various PI's

could coordinate submission of non-local SAE documentation and sponsor amendments. The Board should be informed of the mechanism for this and all changes to a protocol should be submitted so as to be effective at all sites simultaneously. Amendments requiring consent form changes would still need to be site specific.

Principal investigators on approved protocols remain responsible for reporting local SAE's to our Board. Annual reviews and amendments will be the responsibility of the CIRB and participating institutions will be notified of any changes in protocol status.

The dates defining the annual review cycle are those fixed by the CIRB. PIs should submit an AHC annual review form to our office at the time they submit the same data (mostly enrollees, attrition, withdrawal, etc.) to the sponsoring organization(s).

Below are materials from the NCI web site ([www.ncicirb.org](http://www.ncicirb.org)) that offer more detail. Included are:

- Local Institution Procedures

- Division of Responsibilities Between NCI's Central IRB and Participating Local Institutions

- FAQ

## **Local Institution Procedures**

- 1) A local investigator at a participating institution who wishes to enroll subjects in a CIRB-approved protocol downloads the protocol, informed consent documents, and the CIRB application, from the Participant side of this website and submits these documents to his/her local IRB.
- 2) Each local IRB designates at least one voting member(s) of the local IRB to conduct the "facilitated review" of the study that the investigator submitted. The role of the person(s) is to determine whether there are local concerns that need to be addressed and whether to accept the CIRB Review. Local IRBs need to comply with OHRP guidance that, "...an institution relying upon another institution's IRB has a responsibility to ensure that the particular characteristics of its local research context are considered through subsequent review by appropriate designated institutional officials, such as the Chairperson and/or other members of its local IRB."
- 3) The designated person(s) examines the materials available on the CIRB web site, and/or such other \ information as they may seek, so they can decide whether a particular protocol and informed consent documents are acceptable and whether they are appropriate in their local context.
- 4) Local IRB policies should specify if that person(s) has more than a "yea or nea" authority, whether they (or other IRB members) can propose/approve additions to the protocol or word substitutions in the informed consent (see next paragraph). Local IRBs have the option to accept the CIRB approval "as is", accept it with de minimus modifications (see below), or they may decide not to accept the CIRB review and require that the investigator submit the protocol for full Board review at their site. If the designated person(s) do not accept the CIRB review they may still utilize CIRB written materials as resources for their local process.
- 5) As part of this "facilitated review", the local IRB may add stipulations or local requirements to protocols, particularly to increase subjects' 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 considered. Local IRBs 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 contents. Per current OHRP/NCI guidance, any informed consent changes must be justified in the IRB minutes and sent to the Cooperative Group administering that protocol.
- 6) The local IRB must notify the Central IRB Administrative Office each time it accepts the CIRB review of a protocol. Clicking on the "Protocol Acceptance" button/link within the main menu for each protocol and then following the directions for completing the Protocol Acceptance Form does this. In order for the CIRB to become the Official IRB of Record for the site for a particular study, this form needs to be completed and submitted. A separate form must be submitted for each protocol review that is accepted.

The CIRB will use this reply to set up a database both for record keeping and notification purposes. The CIRB will notify the local IRB when there are any actions taken on the protocol, e.g., an SAE report provoking a change in the consent form, an approved protocol amendment, a change in the protocol/informed consent resulting from the Continuing Review, etc.

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## **Division of Responsibilities Between NCI's Central IRB and Participating Local Institutions**

The Central Institutional Review Board (CIRB) Initiative is a pilot project sponsored by the National Cancer Institute (NCI) in collaboration with the DHHS Office of Human Subjects Protection (OHRP) to

develop an innovative approach to human subjects protection for national multi-center trials in cancer. The primary goals of the Initiative are

- To improve access to clinical trials for patients and their physicians by enabling local IRBs to rapidly approve NCI sponsored multi-site trials through the use of a facilitated review process;
- To enhance the protection of research participants by providing consistent expert IRB review at the national level before the protocol is distributed to local investigators;
- To collaborate more effectively with local IRBs thus allowing them to focus on the actual conduct of research at their ethical conduct of human research; and
- To reduce administrative burdens on local IRBs and investigators associated with IRB submission.

The NCI's CIRB differs from typical commercial IRBs in some important ways. Most commercial IRBs review and manage pharmaceutical company trials and must adhere to FDA regulations only. Federally sponsored human research, such as NCI sponsored trials, must adhere to OHRP regulations as well as FDA regulations. The OHRP regulations and guidance require that when an IRB is reviewing on behalf of another IRB, the reviewing IRB must have an understanding of the local context in which the research takes place. In order to meet the "local context" requirement, NCI has created a collaborative model with the local IRBs in the pilot in which the local IRB decides whether to accept the CIRB review in light of any local concerns. OHRP has agreed that this review can be conducted by the local IRB chair or a subcommittee, does not require full Board review, and therefore can occur as quickly as the local decision-makers deem appropriate.

The following division of responsibility is based on the premise that the CIRB's primary function is *initial and continuing review of protocols* and that the local institution's primary function is *consideration of local context and oversight of local performance* for these protocols. The local institution, through its own local IRB, will decide on a protocol-by-protocol basis whether to accept the review of the CIRB or to conduct its own review of the protocol.

*The responsibilities of the CIRB are to:*

- 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;
- 2) Maintain and make accessible to a designated local IRB at the local institution the CIRB application, protocol, informed consent, primary reviews, minutes, notification letters, and correspondence from Groups.
- 3) Carry out Continuing Reviews, reviews of 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;
- 4) Notify each local institution that has accepted the CIRB review of any new materials that have been reviewed for an active protocol and any changes in the protocol approval status;
- 5) Maintain an OHRP approved Assurance for human subjects research;
- 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;

- 7) Make available to the local institution the roster of CIRB membership and the CIRB Standard Operating Procedures and policies;
- 8) Ensure that CIRB members receive proper initial and continuing education on topics relevant to human subjects protections;
- 9) Notify the local institution immediately if there is ever a suspension or restriction of the CIRB's authorization to review protocols; and
- 10) Notify the local institution of any CIRB policy decisions or regulatory matters 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, any major protocol violations, and any 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 should be shared with the CIRB and reported as required by the procedures established by the protocol's sponsoring Group;
- 2) Ensure that the investigators and other staff at the local institution who are conducting the protocol are appropriately qualified and meet the institution's standards for eligibility to conduct research;
- 3) Provide to the CIRB and keep current the names and addresses of local contact persons who have authority to communicate for the local IRB, such as the local IRB administrator;
- 4) Establish a procedure by which the local IRB will receive and review the CIRB materials for protocols to be performed at the local institution. For each CIRB reviewed protocol (approval or disapproval) that is submitted to the local IRB by a local investigator:
  - Review the CIRB's materials;
  - Determine if there are any local context issues that must be addressed by the local IRB;
  - Decide whether to accept the CIRB review or conduct a separate local IRB review.

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;

- 5) 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;
- 6) If the local IRB accepts the CIRB approval of a protocol, maintain in the local IRB records documentation of the decision and evidence that it has received and considered all CIRB material relevant to the protocol;
- 7) Maintain an OHRP approved Assurance for human subjects research;

- 8) Maintain a local IRB whose membership satisfies the requirements of 45 CFR 46;
- 9) Maintain a human subjects protection program, as required by the DHHS OHRP;
- 10) Ensure that local IRB members and local investigators receive proper initial and continuing education on the requirements related to human subjects protections;
- 11) Notify the CIRB immediately if there is ever a suspension or restriction of the local IRB's authorization to review protocols; and
- 12) Maintain compliance with any additional state, local, or institutional requirements related to the protection of human subjects.