NCI’s CIRB: Streamlining IRB Processes
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Agenda
• Background of Initiative
• Enrollment and Utilization Data
• Evaluations – past, present, future
• How it works

The NCI CIRB Initiative - Background
Established in 1999 as recommended in the Armitage Report from the NCI’s Clinical Trials Program Review Group:
• Help NCI create a more efficient and effective clinical research effort
  – Streamline or eliminate redundant processes and procedures
http://deainfo.nci.nih.gov/ADVISORY/bsa/bsa_program/bsactprgmin.htm

Target questions:
– Primary: Could a CIRB reduce the significant local administrative burdens for multi-site trials while maintaining a high level of human subjects protection
– Secondary: Would a CIRB enhance the protection of research participants by providing consistent expert IRB review at the national level before the study is distributed to local investigators

The NCI CIRB Initiative - Background (continued)
• Initial/start-up phase
  – Frequent consultations with OHRP
  – Review model decision
    • OHRP (OPRR) allows for different centralized IRB models
        http://www.hhs.gov/ohrp/humansubjects/guidance/local.htm
    • Model A
      – Appropriate where no local IRB exists
      – Understanding of local context obtained via site visits, audits, teleconferences
    • Model B
      – More appropriate where local IRB already present
      – Can utilize LIRB for understanding of local context
      – No need for site visits, etc.

The NCI CIRB Initiative - Background
• Initial/start-up phase (continued)
  – NCI chose Model B where CIRB and LIRB share regulatory responsibilities – a partnership
    • CIRB’s primary function is initial and continuing review of studies, including amendments and Group-distributed unanticipated problems
    • The local institution’s primary function is consideration of local context, oversight of local performance, review of locally occurring adverse events
  – Developed a new review term called “Facilitated Review” – the review during which the local IRB reviews the CIRB-approved study for local context considerations.
## Adult Board Composition

- One Chair and 15 Voting Members (16 total)
- **Patient Advocates**: 19% (3)
- **Physicians**: 44% (7)
- Other Professionals: 37% (6)
  - Nurses 2
  - Pharmacists 2
  - Statistician 1
  - Ethicist 1

Source: EMMES  
Current as of 03/25/2010

## Enrollment and Utilization Data Summary

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number of Enrolled Institutions</td>
<td>346</td>
</tr>
<tr>
<td>Total Number of Enrolled Institutions including other institutions relying on their IRB</td>
<td>753</td>
</tr>
<tr>
<td>Number of Studies Available for Facilitated Review</td>
<td>153</td>
</tr>
<tr>
<td>Number of Facilitated Reviews utilized (adult only)</td>
<td>10,410</td>
</tr>
</tbody>
</table>
  - Adult Studies | 6,536 |
  - Pediatric Studies | 3,874 |

Source: EMMES  
Current as of 02/28/2010

## Evaluations Performed

- **External Evaluation Panel recommended four components of evaluation plan**
  1. Maintain metrics of Enrollment and Utilization  
     - Ongoing from beginning of Initiative
  2. Satisfaction Surveys (local site IRB and research staff)
     - Conducted by Research Triangle Inc. of Washington, DC in 2005
       - 60% felt that participating in the CIRB saved them some or a lot of time and effort
       - Overall experience mean 65% good - very good
  3. Cost Analysis - Todd Wagner, PhD, Stanford University economist
     - Published in _Journal of Clinical Oncology_ Feb. 2010
     - [http://jco.ascopubs.org/cgi/content/full/28/4/662](http://jco.ascopubs.org/cgi/content/full/28/4/662)
  4. Obtain AAHRPP Accreditation
     - In progress

## Additional Evaluation Information

- **“Barriers to Using CIRB” Survey and Analysis**
  - Conducted by Science and Technology Policy Institute
  - Recommended pursuing AAHRPP Accreditation
  - Encouraged development of a model SOP for incorporating CIRB into local processes
  - Was completed and is posted at the following URL: [http://www.ncicirb.org/CIRB_Enrollment_Packet.asp](http://www.ncicirb.org/CIRB_Enrollment_Packet.asp)

- **Costs and Benefits of CIRB (Todd Wagner, PhD, Stanford University economist)**
  - Observational study comparing sites using the CIRB with sites
  - Use of CIRB resulted in faster reviews and reduced IRB and research staff time and effort
  - Total savings is higher when CIRB used as intended
Investigator Perspective

- IOM National Cancer Policy Forum: Multi-Center Phase 3 Clinical Trials and NCI Cooperative Groups, July 2008
  - promoted use of the CIRB as key to reduce redundancy, cost, variability, time and to increase oversight and safety
  - encouraged mandating use of CIRB

Research Staff Perspective

- Hahn, Kimberly. Measuring IRB Efficiency: Comparing the Use of the National Cancer Institute Central IRB to Local IRB Methods, SoCRA SOURCE, May 2009
  - “Retrospective analysis demonstrated an increase in productivity with fewer staff hours after initiation of the Central IRB.”
  - “IRB process is most efficient and provides increased benefits in terms of time, costs, and patient safety, as well as other measures when Central IRB is utilized.”

How does the NCI CIRB model work for local IRB and investigators/research staff?

- Local investigator is notified of new study via:
  - Routine Group/CTSU activation announcement
  - CIRB semi-monthly “Website Posting Summary” email
- If the local investigator decides to open study:
  - OPTION 1: Investigator or CRA downloads the completed application, protocol, and informed consent document from the CIRB website and submits documents to local IRB
  - OPTION 2: IRB staff download all the documents and submit to IRB Chair or Subcommittee for review

How does the NCI CIRB model work – site?

- Chair/subcommittee assesses CIRB review documents and decides whether local considerations are addressed (called “facilitated review”)
  - If local considerations are not addressed, must review study per local procedures
  - If local considerations are addressed, accepts facilitated review and notifies CIRB via CIRB Website
- The CIRB becomes the IRB of record for study at that site and is responsible for reviewing amendments, continuing reviews, unanticipated problems distributed by the Group, recruitment materials, etc.

Facilitated Review - Initial Review Overview

- Cooperative Group Distributes Study
- Local Investigator Decides to Open Study
- CRA or Investigator Downloads study Documents from CIRB Website
- Local IRB Chair/Subcommittee Reviews CIRB Documents and Decides to Accept Facilitated Review
- Local IRB Reports Facilitated Review Acceptance to the CIRB via the CIRB Website
- CIRB is IRB of Record for the Study; Local Investigator May Begin Research

Overview of CIRB Processes: Continuing Review

- Continuing Review is conducted by the CIRB; Local IRB is not required to review.
- Continuing Review is completed by the CIRB at least 45 days in advance of the expiration date (no risk of lapse in approval).
- CIRB may request changes at the time of continuing review.
  - CIRB sites simply download the approved continuation from the CIRB website.
  - Non-CIRB sites will need to submit an amendment to their Local IRB.
Overview of CIRB Processes: Amendment Review

- Amendment Reviews are conducted by the CIRB; Local IRB is not required to review.
- CIRB Amendment Review takes place prior to activation of the amendment by the Cooperative Group.
- CIRB posts amendment and related documents at the time of Cooperative Group activation.
- CIRB sites download the approved amendment from the CIRB website.
- Non-CIRB sites must submit the amendment to their local IRB.

What to expect when enrolling in the CIRB?

Enrollment Form and Authorization Agreement

- Important local institution information to be included on the Enrollment Form:
  - Names of IRB(s) that review NCI Cooperative Group clinical trials
  - Names of other institutions that rely on those IRBs for review of Cooperative Group trials, if any
  - Contact information for local investigator(s), research staff, and IRB

- Authorization Agreement:
  - States that the “reviews, approvals, and continuing oversight performed by the NCI CIRB satisfy the requirements of the DHHS regulations for the protection of human subjects as 45 CFR 46…”
  - Requires institution to sign indicating their agreement to rely on the CIRB reviews as outlined in the ‘Division of Responsibilities’ document
  - Include IRBs relying on institution’s IRB
  - Send two original, signed documents for NCI to execute

Communications

- Identify all IRB and research staff that will need access to the CIRB website
  - Everyone identified will receive user names and passwords
  - IRB office staff who are designated by the IRB to accept facilitated review have unique level of access
- Broadcast emails which include the semi-monthly Website Posting Summary, if desired
- Other communication pathways
  - NCI CIRB website (www.ncicirb.org)
  - Frequently Asked Questions available on the website
  - CIRB Helpdesk 1-888-657-3711 or ncicirbcontact@emmes.com

CIRB - Benefits of Participation

- Research Participants
  - Oncology-specific multidisciplinary Board
  - Dedicated review for study participant protections
  - Facilitated review allows local sites to open studies within days
  - Encourages sites to consider opening studies in rare diseases for those patients

- Investigators/Research Staff and IRBs
  - Streamlined processes
    - Reduced workload – fewer submissions and reviews
    - Completed IRB Application provided
  - Elimination of full Board review
    - Reduced workload on local IRB members
  - Decreased local IRB time and costs
    - CIRB becomes the IRB of record for the complete life-cycle of the protocol – advantages are cumulative over the many years a phase 3 study lasts

CIRB Website Tour

- Tour of the following:
  - Homepage
  - Restricted-access “Participant’s Area”
  - RTOG 0617
    - Initial Review
    - Amendment Review
    - Continuing Review
    - SAE Review
The NCI CIRB Initiative – Summary of Rationale

- Emphasis on speed of trial activation, while important, is but one factor to consider regarding the IRB process
- Other factors include:
  - IRB costs of review
  - Physician/nurse/CRA time to complete IRB application; duplicate IRB submission, etc.
  - IRB members’ time and effort
  - Number of patients at a site with specific cancer
    - Easier to open clinical trials for rare diseases

6 Easy Steps – Summary of Enrollment

- Complete the CIRB Enrollment Form
- Modify institution’s FWA to include the CIRB
- Sign the Authorization Agreement
- Return Enrollment Form/Auth. Agreement to CIRB
- Create a local IRB SOP for utilizing the CIRB
- Notify local investigators of the new process

Contact the NCI CIRB

Website: http://www.ncicirb.org
Email: ncicirbcontact@emmes.com
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