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NCI's CIRB: Streamlining IRB Processes

Presented to
Southwest Oncology Group
Clinical Research Associates

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Agenda

- Background of Initiative
- Enrollment and Utilization Data
- Evaluations – past, present, future
- How it works

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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

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The NCI CIRB Initiative - Background

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

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The NCI CIRB Initiative - Background

- Initial/start-up phase
 - Frequent consultations with OHRP
 - Review model decision
 - *OHRP (OPRR) allows for different centralized IRB models*
 - See Guidance of August 27, 1998 (updated July 21, 2000) entitled "Knowledge of Local Research Context" <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.

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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.

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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

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Adult Board Composition

- The most current membership roster is available on the CIRB website at: http://www.ncicirb.org/cirb_roster_brief.asp



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Enrollment and Utilization Data Summary

- Total Number of Enrolled Institutions **346**
- Total Number of Enrolled Institutions including other institutions relying on their IRB **753**
- Number of Studies Available for Facilitated Review (adult only) **153**
- Number of Facilitated Reviews utilized **10,410**
 - Adult Studies: 6,536
 - Pediatric Studies: 3,874

Source: EMMES Current as of 02/28/2010

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Adult Institutions Conducting 50 or more Facilitated Reviews

| | |
|--|---|
| 1. Advocate Health Care Network Institutional Review Board (AHCNIRB) | 16. Provena St. Mary's Hospital |
| 2. Aulman Hospital | 17. Providence Hospital |
| 3. Aurora Health Care | 18. SUNY Upstate Medical University |
| 4. Borgess Medical Center | 19. Saint Joseph Mercy Health System |
| 5. Bronson Methodist Hospital | 20. St. James Hospital and Health Centers |
| 6. Georgetown University | 21. St. Vincent Hospital |
| 7. Greater Baltimore Medical Center, Inc. | 22. Thomas Jefferson University |
| 8. Gundersen Clinic, Ltd. | 24. University Medical Center of Southern Nevada |
| 9. Marshfield Clinic | 24. University of New Mexico Health Sciences Center |
| 10. Mission Hospitals, Inc. | 25. Via Christi Regional Medical Center |
| 11. Mt. Sinai Medical Center | 26. Washington University School of Medicine |
| 12. Nevada Cancer Research Foundation CCOP | 27. West Michigan Cancer Center |
| 13. Northeast Georgia Health System, Inc. | |
| 14. Ochsner Clinic Foundation CCOP | |
| 15. Oltumwa Regional Health Center | |

Current as of 02/28/2010

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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
 - 80% felt that participating in the CIRB saved them some or a lot of time and effort
 - Overall experience = 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>
 - 4) Obtain AAHRPP Accreditation
 - In progress

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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
- Costs and Benefits of CIRB (Todd Wagner, PHD, Stanford University economist)**
 - Observational study comparing sites using the CIRB with sites using local IRB for review
 - 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

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Investigator Perspective

- IOM National Cancer Policy Forum: Multi-Center Phase 3 Clinical Trials and NCI Cooperative Groups, July 2008
 - *Alan Keller, MD, Cancer Care Associates, "Multi-site Clinical Trials in the Community: Models and Methods: What Works, What Doesn't and Why"*
 - 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."*

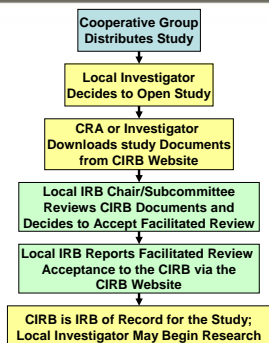
How does the NCI CIRB model work for local IRB and investigators/research staff?

- 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



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

What to expect when enrolling in the CIRB? 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

CIRB - Benefits of Participation (continued)

- 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

Welcome to the NCI Central Institutional Board Review (CIRB) Initiative - Microsoft Internet Explorer

The Central Institutional Review Board Initiative
in consultation with OHRP

Home | How to join | Studies | Participant's Area | FAQs | Contacts | The CIRB Initiative | Board Members | Feedback | How it works | Meeting Info | Links | Activity Updates

Welcome to the Central IRB Initiative
partnering with local IRBs

The Central IRB (CIRB) Initiative is designed to help reduce the administrative burden on local IRBs and investigators while continuing a high level of protection for human research participants.

A local IRB's use of the CIRB facilitated review mechanism enables an investigator to enroll patients into adult and pediatric Cooperative Group clinical trials significantly faster than when employing traditional method of IRB review.

The CIRB Initiative is sponsored by NCI in consultation with the Department of Health and Human Services Office for Human Research Protections (OHRP).

What's New

- **NEW CIRB Changes to Initial Review Process and ICDs for Adult Trials**
- **NEW CIRB Website Postings Summary (07/14/2009)**
- **CIRB Study Activity Update (06/15/2009)**
- **CIRB Study Activity Update (05/21/2009)**
- **CIRB Study Activity Update (05/15/2009)**
- **CIRB Study Activity Update (04/29/2009)**

22 more what's new

How to Join

back to top

Click here for Facilitated Reviews previously accepted at your institution

CIRB Studies List | NCI Document Page | Adult Meeting List | Pediatric Meeting List

All fields are optional. The criteria specified will be used to form an "AND" statement for the search. The result will be displayed in a table format on the lower portion of the web page.

Search Criteria for Study List

Choose a Group: SWOG
 Choose a Study #: SWOG-S0518
 Enter a Group Activation Date Range: (start) (end)
 Search keywords within a Study title

Display Criteria for Study List

Display by: Study Number

Search Clear Criteria Additional Help

Quick Group List

ACOGOG | CALGB | COG | ECOG | GOG | HCOGT | NCIC CTG | NEAMP | RTOG | **SWOG**

Email CIRB contact to send your thoughts and questions to the CIRB

| Study # | Study Title | CIRB Initial Review Date | Group Activation Date | Expiration Date |
|------------|---|--------------------------|-----------------------|-----------------|
| SWOG-S0518 | Phase III Prospective Randomized Comparison of Depot Octreotide plus interferon Alpha versus Depot Octreotide plus Bevacizumab (NSC 704865) in Advance, Poor Prognosis Carcinoid Patients | 10/12/2007 | 12/1/2007 | 9/2/2010 |

SWOG-S0518 Phase III Prospective Randomized Comparison of Depot Octreotide plus interferon Alpha versus Depot Octreotide plus Bevacizumab (NSC 704865) in Advance, Poor Prognosis Carcinoid Patients (Back to Study List)

Current Study Documents (view/print documents)

Protocol/Informed Consent Documents

- Protocol Version Date 10/29/09
- CIRB's Informed Consent Document for Protocol Version Date 10/29/09 [Rev3]

To download the Local IRB Facilitated Review Packet click here.

In order for the CIRB to be the IRB of Record for this study at your site, you must:

1. Conduct Facilitated Review 2. Submit the Facilitated Review Acceptance Form (click here), which informs the CIRB of your request for it to be the IRB of Record.

Initial Review | Amendment Reviews | Continuing Reviews | **SAE Reviews** (Back to Study List)

Initial Review 2007

- Protocol
 - o Protocol Version 09/04/07
 - o Protocol Version 07/25/07
 - o Protocol Version 02/03/07
 - o Protocol Version 07/28/06
- Informed Consent
 - o Informed Consent for Protocol Version 09/04/07
- CIRB Application
 - o CIRB Initial Review Application (Protocol Version 09/04/07)

SWOG-S0518 Phase III Prospective Randomized Comparison of Depot Octreotide plus interferon Alpha versus Depot Octreotide plus Bevacizumab (NSC 704865) in Advance, Poor Prognosis Carcinoid Patients (Back to Study List)

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CIRB Acknowledgement - Re-opening of Registration Step 2

- Correspondence
 - o 02/24/10: CIRB Acknowledgement of SWOG-S0518 Re-opening of Registration Step 2 (the SPECT Substudy) to Accrual
 - o 02/15/10: SWOG Re-opening of Registration Step 2 (the SPECT Substudy) to Accrual Memo

CIRB Acknowledgement - Temporary Closure to Step 2 (SPECT Substudy)

- Correspondence
 - o 01/28/10: CIRB Acknowledgement of SWOG-S0518 Temporary Closure to Step 2 (SPECT

SWOG-S0518 Phase III Prospective Randomized Comparison of Depot Octreotide plus interferon Alpha versus Depot Octreotide plus Bevacizumab (NSC 704865) in Advance, Poor Prognosis Carcinoid Patients (Back to Study List)

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Initial Review | Amendment Reviews | Continuing Reviews | **SAE Reviews** (Back to Study List)

Continuing Review September 2009

- Continuing Review Forms
 - o CIRB Continuing Review Application (Protocol Version Date 02/20/09)
- Correspondence
 - o 02/09/09: CIRB Continuing Review Approval Letter (Protocol Version Date 02/20/09)
 - o 07/06/09: Continuing Review Reminder Notice
- Protocol
 - o Protocol Version Date 02/20/09
- Informed Consent
 - o CIRB's Informed Consent Document for Protocol Version Date 02/20/09 (CP09)

Initial Review | Amendment Reviews | Continuing Reviews | **SAE Reviews** (Back to Study List)

SAE Reviews

Recommended Board Action Code:

- 1 No Changes to Informed Consent Document and/or Protocol
- 2 Informed Consent Document Requires Clarification of Existing Risk
- 5 CTEP Action Letter Awaiting Group's Amendment
- 12 New Risk Identified Not Currently in Informed Consent Document: Request Validation
- 13 New Risk Identified Not Currently in Protocol: Request Validation
- 14 New Risk Identified Not Currently in Protocol and Informed Consent Document: Request Validation
- 15 Need more information - AE Report Contains Preliminary Information and a Determination Cannot be Made
- 99 Review Pending

* Data Report Received From Group column will display data going forward 1/15/2009

| AE# (To not be AE# by SAE number, please click the "AE" link above) | Agent | Applicable Studies | Primary Event | Report Date | Date Report Received or Obtained from Group/Lead Group* | Date Sub Code Review | Rec Code | Rationale for Recommendation | Date Full Board Review | Full Board Final Action |
|---|-------------|--------------------|---|-------------|---|----------------------|----------|------------------------------|------------------------|---|
| 1232128 | bevacizumab | SWOG-S0518 | Gr. 5: Hemorrhage, pulmonary/upper respiratory; Lungs; Gr. 4: pneumonia/pulmonary infiltrates | 07/09/09 | 08/02/09 | 11/30/09 | 1 | In the ICD. | 12/17/09 | No Changes to Informed Consent Document and/or Protocol |

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
CIRB Toll-free Number: 888-657-3711
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