The NCI Central IRB Initiative

Third Annual Medical Research Summit

Washington, D.C.

March 2003

The NCI CIRB Initiative

- **Began August 1999 in consultation with OHRP (OPRR)**
- **To establish a Central IRB for NCI Phase 3 multi-center trials**
  - **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 determine whether a CIRB could eliminate the significant local administrative burdens for multi-site trials while maintaining a high level of human subjects protection**

Selecting a CIRB Model

- **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://ohrp.osophs.dhhs.gov/humansubjects/guidance/local.htm

- Model A
  - Appropriate where no local IRB
  - 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.

- NCI chose Model B for practical reasons
  - Unlike many other CIRBs, the NCI CIRB does not exist in lieu of a local IRB
  - Local IRBs already exist and NCI must interface with them
  - Who better to understand local research context than local IRB chair/members?
  - Refer to it as the “facilitated review” model
  - Envisioned pilot as 25-30 sites; with success would expand to all the institutions in the Cooperative Groups

How does the facilitated review model work?

- CIRB approves protocol
- Local investigator is notified of protocol via
  - Routine Group activation announcement
  - CIRB e-mail

- If the local investigator decides to open protocol, s/he downloads the completed application, protocol and consent from the CIRB website
- Investigator submits documents to local IRB

- Local IRB office downloads all CIRB review materials: primary reviews, detailed minutes, correspondence, etc.
- Local chair/subcommittee reviews for local concerns and decides whether to approve

- If LIRB accepts, they notify CIRB.
- The CIRB becomes the IRB of record. It handles amendments, continuing reviews, adverse events etc.
- If it does not accept, LIRB can decide to review the protocol themselves as per their own local procedures.

Division of Responsibilities

- **CIRB and LIRB share regulatory responsibilities; the CIRB is not an additional IRB layer**
- **The CIRB's primary function is *initial and continuing review* of protocols**
- **The local institution's primary function is *consideration of local context and oversight of local performance***

Current Status

- NCI holds an FWA
- NCI Director appoints diverse Board
- Meeting monthly since January 2001
- Menu includes all Phase 3 Adult Cooperative Group protocols (30-40 per year)
- Daily administrative operations managed by contractor

- Recent expansion
  - Original number of sites was too small for meaningful data
  - Invitation letter sent to local IRBs
- Target recently met: 111 participating local IRBs
  - Both community hospitals and university teaching hospitals (see website for list)

Total number of protocols reviewed: 42

# of protocols with facilitated review: 31
# of sites accepting at least one review: 23
Total # of facilitated reviews: 93

Recent expansion to 111 participating IRBs (representing 126 participating institutions)

- 40 of top 400 accruing cooperative group sites are in Initiative
- Cancer centers including Columbia, Fox Chase, Washington University, Georgetown, University of Colorado

- Emphasis shifting from expansion to utilization for the next 12-18 months
  - Communications campaign
  - Outreach to investigators at participating sites
  - Service to LIRBs
- Must utilize facilitated review for project to succeed

Evaluation Plan

- Measure local utilization of facilitated review process
- Quantify CIRB effect on local site time frames
- Assess the experience with CIRB processes of the local IRB Chair, LIRB Coordinator and Principal Investigator (for Cooperative Groups), and CIRB members

- Evaluate the quality of CIRB reviews
- Demonstrate CIRB compliance with federal regulations

Current Challenges

- **Broader experience with facilitated review**
  - **Plan to increase number and range of participating local IRBs**
    - **Perception of liability remains an issue**
- **Continued improvement in review time**
  - **Has decreased over time with experience**

- Complex interactions with LIRBs, Cooperative Groups, Investigators, OHRP
  - Enhanced communications processes
    - With investigators, LIRBs, patient advocacy groups
    - Ongoing meetings with OHRP
- Continued simplification of processes for investigators
  - Online access to IRB application materials to ease process of IRB submission

NCI CIRB: POTENTIAL IMPACT

- LESS BURDEN FOR IRBs
  - Substantial reduction of duplicative review
  - Potentially >500 IRB reviews for large Phase 3 trials
- FASTER ACTIVATION OF TRIALS
  - Within days of IRB application rather than weeks to months
- LESS BURDEN FOR INVESTIGATORS
- MORE TRIALS OPEN PER SITE
  - Greater access for patients and physicians
- TRIALS IN RARE DISEASES BECOME FEASIBLE

KEYS TO SUCCESS

- **TIMELY CIRB APPROVAL**
- **ACTIVE SITES OPENING STUDIES**
- **USE OF FACILITATED REVIEW**

www.ncicirb.org