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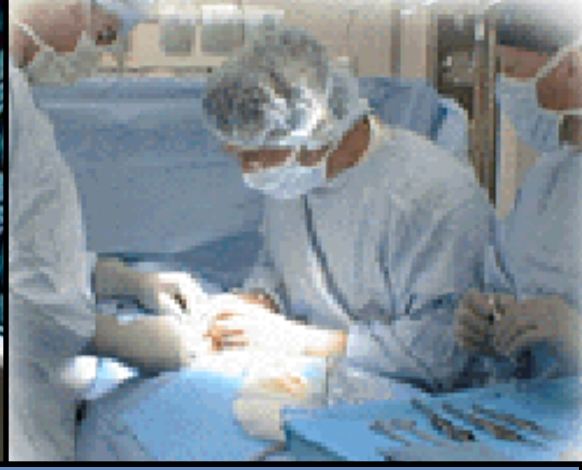

Central Institutional Review Board (CIRB):

Revised Procedures, Accreditation Update, & Cost-Benefit Analysis

Meg Mooney, MD, Jacquelyn Goldberg, JD, and Todd H. Wagner, PhD

Clinical Trials Advisory Committee Meeting

November 4, 2009

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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CIRB: Overview of Presentation

- Revised Procedures for Initial Review of Phase 3 Trials by Adult CIRB
  - Meg Mooney, MD
- Accreditation Update for Adult & Pediatric CIRB
  - Jacquelyn Goldberg, JD
- Cost-Benefit Analysis
  - Jacquelyn Goldberg, JD, NCI, CIB, CTEP, DCTD
    - goldberj@mail.nih.gov
  - Todd Wagner, PhD, VA Palo Alto & Stanford University
    - twagner@stanford.edu

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CIRB: Revised Initial Review Procedures

- Improve timelines for initial review by the Adult CIRB
- Allow activation of study by sites not participating in Adult CIRB as soon as possible
- Promote dialogue about important human subjects protection issues related to trials

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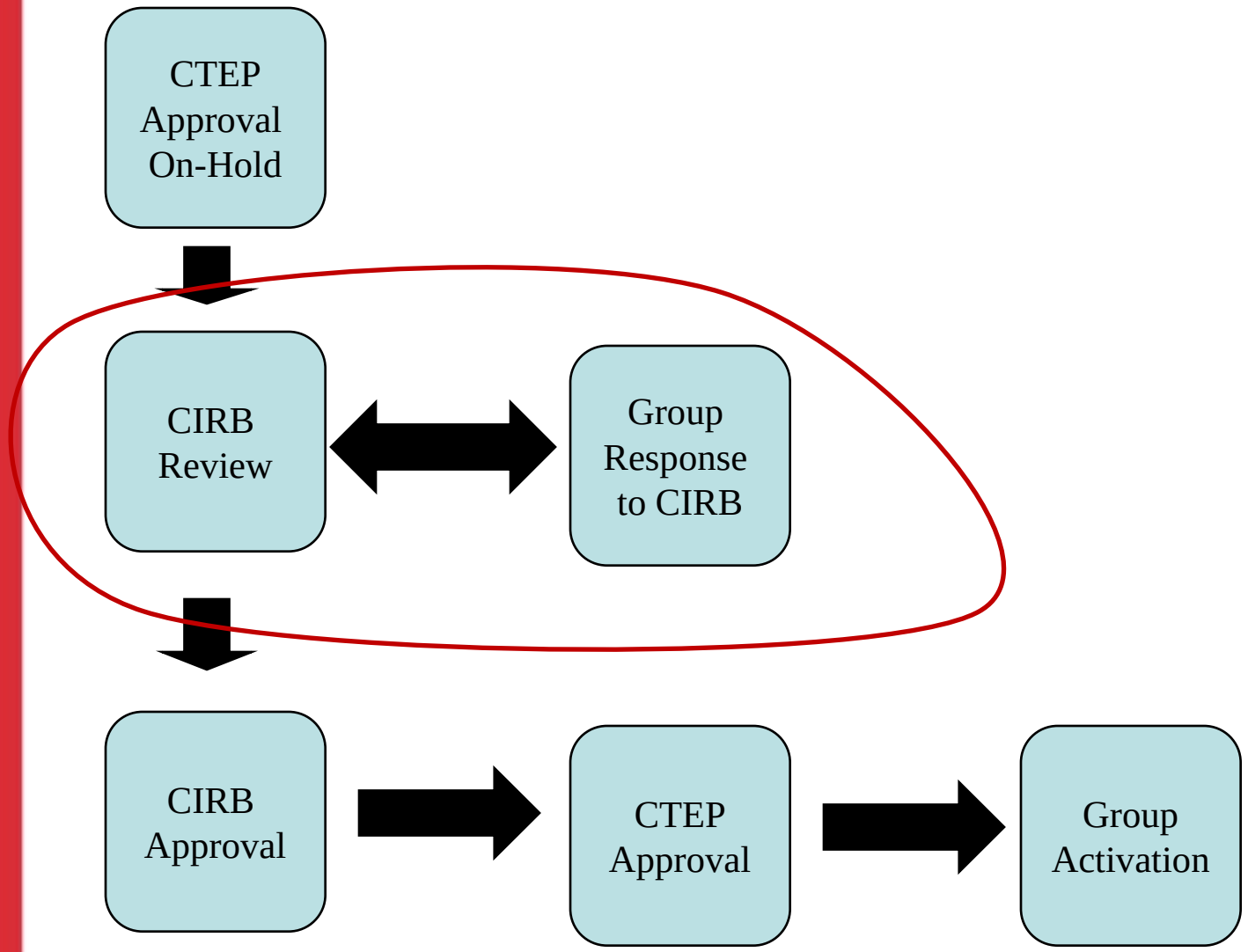
CIRB: Legacy (Sequential) Process for Initial Review



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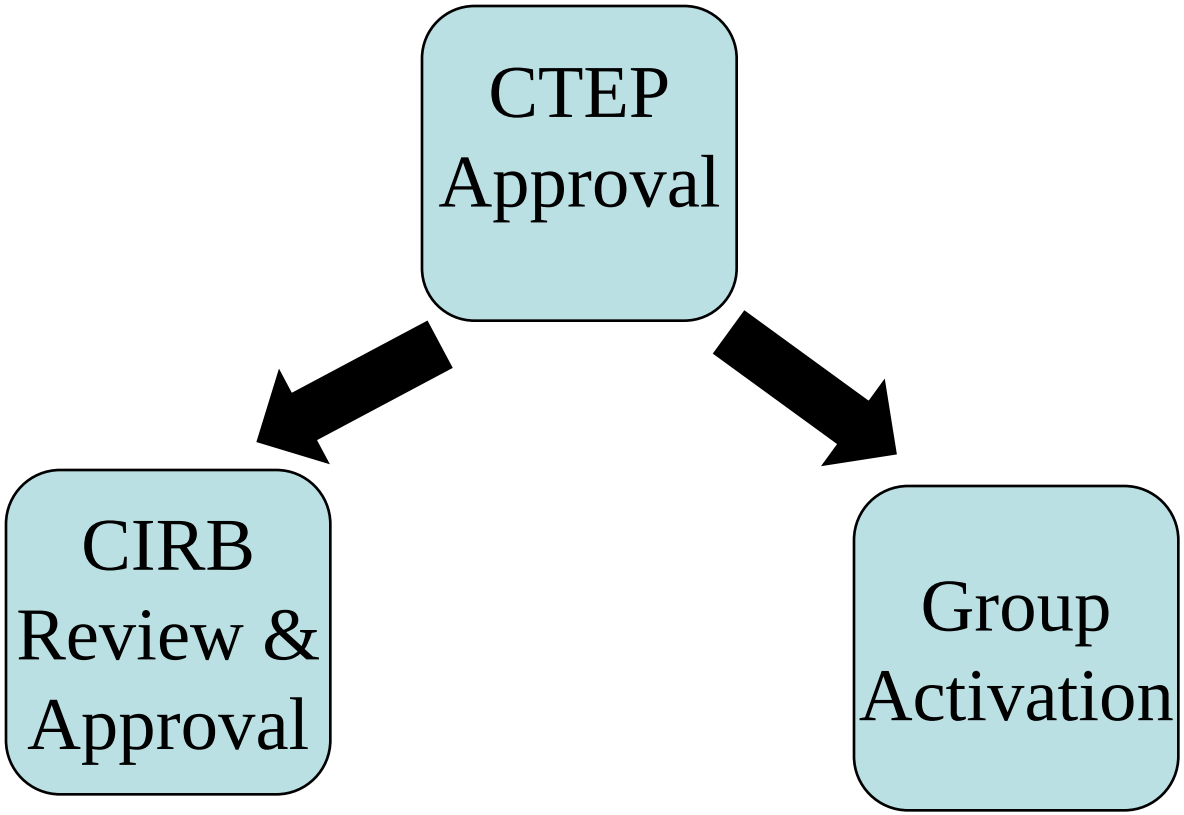
CIRB: New (Parallel) Process for Initial Review (aka C-PIRAT)



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Revised Procedures Include Multiple Changes in Addition to Parallel Review

- Mutually agreed upon timelines by Group, CIRB, and CTEP
- Revamped internal CTEP & CIRB processes
- Adult CIRB has own Informed Consent Document (it may differ from Model ICD per NCI and Group SOPs)
- Improved communication
  - Group, PIs, CTEP (CIB), and CIRB address any outstanding questions at time of CIRB Initial Review Board Meeting / teleconference
  - CTEP review of CIRB Outcome Letters with PRN teleconference(s) to resolve any outstanding issues

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Revised Procedures Include Multiple Changes in Addition to Parallel Review

- Goal – Minimize CIRB stipulations by resolving issues in real time

- Protocol 'Consultants'
  - Groups: Study PI, Study Statistician, others
  - CTEP: CIB Physician, BRB Statistician

Of Note: The last 7 CIRB Study Outcome Letters have been limited to Informed Consent Issues not requiring an amendment; CIRB had no protocol stipulations

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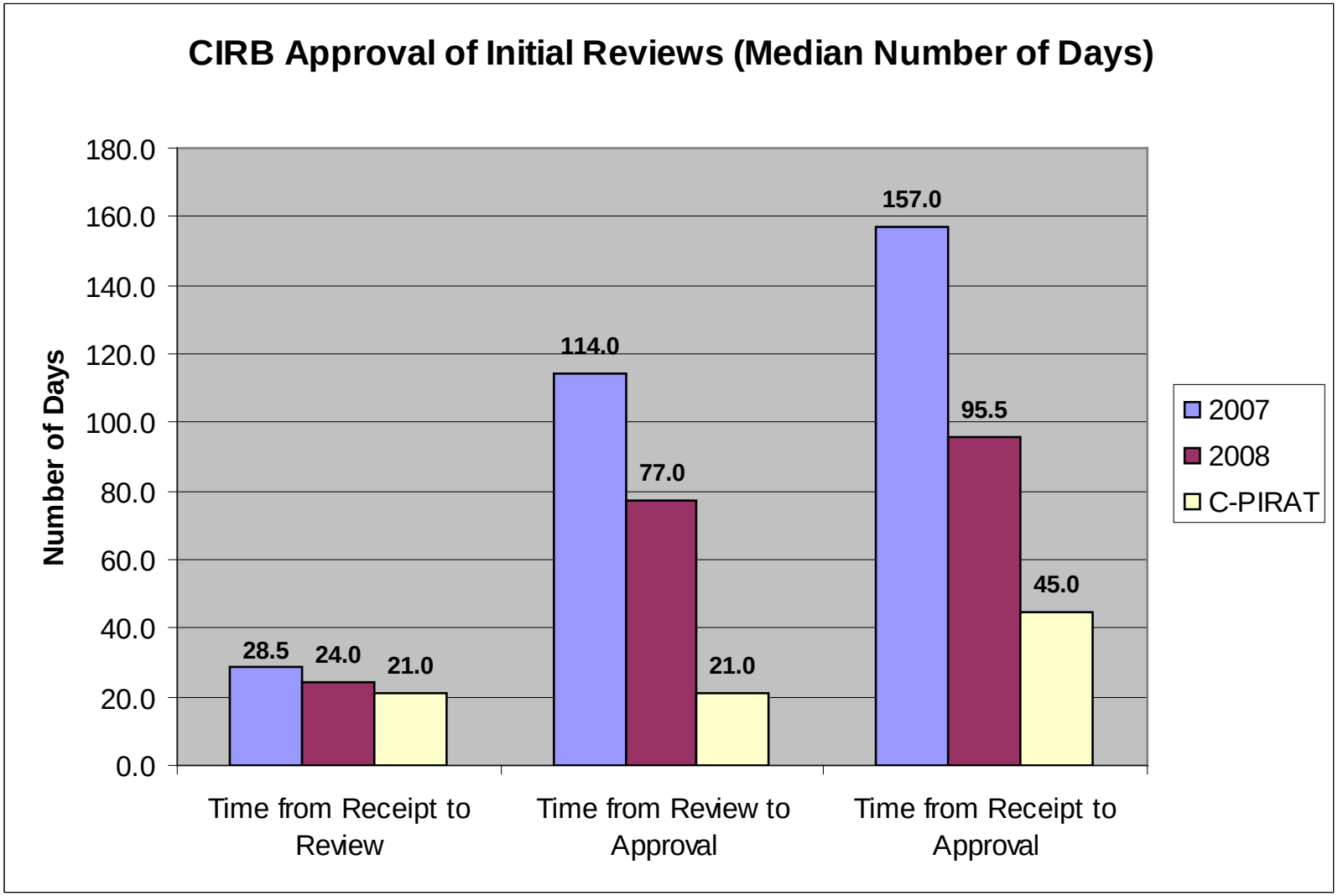
Sample Metrics: Timeline Comparison



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Timeline Comparison

- 2007
  - 16 Initial Reviews Completed
  - Time to approval
    - Range 93 to 447
    - Median 157
- 2008
  - 12 Initial Reviews Completed
  - Time to approval
    - Range 51 to 264 days
    - Median 95.5 days
- C-PIRAT (initiated 5/1/9)
  - 9 Initial Reviews Completed as of 11-24-09 (1 in queue)
  - Time to approval
    - Range 31 to 55 days
    - Median 45 days

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CIRB Approval vs. Study Activation

Of the first 9 trials reviewed through C-PIRAT:

- 6 had CIRB approval prior to Group Activation
- 3 had CIRB approval post-Group Activation
  - CIRB approval was within 17 to 37 days of Group Activation

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AAHRPP Accreditation

- Association for the Accreditation of Human Research Protection Programs (AAHRPP) accreditation the gold standard for IRBs
  - CIRB Evaluation Advisory Panel recommended CIRB become accredited to establish quality benchmark
  - Accreditation is an asset for recruitment
- Process has begun
  - Paid fee
  - Met several times with AAHRPP leadership
- EMMES .50 FTE devoted to effort
- Timeline estimate completion 1 year

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AAHRPP Accreditation Steps

- **Conduct Self-Assessment**
  - Evaluate Human Research Protection Program and make improvements; this often takes 9-12 months; AAHRPP wants to work with us during this phase rather than wait until the application submission
- **Prepare and submit application**
  - a short application form, a program overview (10 page maximum), copies of documents used by the CIRB, and an index to those documents
- **AAHRP site visit**
  - A team of experts reviews submitted materials and schedules an on-site visit
  - During the visit, the team evaluates the CIRB program's performance with respect to the AAHRPP accreditation standards

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AAHRPP Accreditation Steps

- AAHRPP's Council on Accreditation Review and Notification
  - Council reviews the application, the Draft Site Visit Report and the NCI's response, and determines accreditation status.
  - Notification of accreditation status
  - AHRPP has accredited 194 organizations so far
- Re-Accreditation
  - Every three years

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CIRB Cost-Benefit Analysis: Background

- In 2006, NCI funded a study to assess time, effort and cost associated with the Central IRB
- PI was Todd Wagner, health economist with Palo Alto VA and Stanford University
- Focused on adult CIRB since pediatric Board was new and there were a small number of affiliated sites

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Objectives of Cost-Benefit Analysis

1) To determine whether participation in the CIRB was associated with lower effort, time and cost compared to not participating in the CIRB

2) To assess whether the CIRB was saving society (taxpayers) money

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Methods for Objective 1: Cost-Benefit Analysis

- Surveyed researchers and IRB staff at affiliated and non-affiliated sites to understand effort and time
  - Asked about most recently approved adult oncology trial
  - Caveat: self-reported data
- Hours of effort were translated into costs using national average wages, education and position
- Response rate:
  - 60% response rate (300/498) research staff
  - 42% response rate (50/120) IRBs

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Results for Objective 1

- For initial reviews, CIRB affiliation was associated with:

Research Staff

- 6.1 hours research staff effort saved
- 34 days faster from the date the research staff started the paperwork until IRB approval
- More predictable initial review times (fewer very lengthy reviews)

IRB staff

- 2.3 hours less effort for IRB staff (p=0.10)
- Use of less expensive staff to review CIRB protocols (p=0.01)

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Results Objective 1: Cost-Benefit Analysis

- Use of CIRB was associated with a savings of $717 per initial review
  - $321 related to research staff savings (p=0.04)
  - $396 associated with IRB staff savings (p=0.014)
- No significant differences for continuing reviews or amendments

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Methods Objective 2: Cost-Benefit Analysis

- Investigated whether the adult CIRB saved money in from "societal" perspective
- Are the average monthly costs of running the CIRB less than the average savings (Avg savings per protocol x # Protocols per month)?
  - Estimated monthly CIRB costs came from personnel data provided by contractor 1/07-06/08
  - Saving per protocol came from Objective 1
  - Protocols per month came from CTSU data from 3/06-5/08

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Results Objective 2: Cost-Benefit Analysis

- CIRB cost approximately $160,000 per month to operate in 2008
- There were approximately 148 initial reviews in CIRB sites per month, for a monthly savings of $106,175 (148 * $717)
- CIRB yielded a societal cost of approximately $55,000 per month in 2008

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Results Objective 2: Cost-Benefit Analysis

- Saving society money is not a conventional goal for health interventions
- Savings would be higher if
  - More sites joined the CIRB
  - Enrolled institutions used the CIRB as intended
- Calculations do not include:
  - Benefit of faster, more predictable reviews
  - Savings of $10 per AE

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Conclusion: Cost-Benefit Analysis

- CIRB appears to save local researchers and IRB staff time and effort
- Increasing enrollment would likely lead to increased savings for society
- This evaluation considers the existing system; enhancing efficiency may be possible

CIRB Update

Questions and Discussion