Children's Hospital of Philadelphia: Recent Changes

Mark S. Schreiner, MD
Chair,
Committees for the Protection of Human Subjects (IRB)

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Recent Changes in CHOP IRB Procedures

- Unchecked the box 2012
  - Expanded Expedited and Exempt categories
  - 3 year approval of Expedited studies
- Change in IRB structure
- Development of totally electronic IRB reviewer form in eIRB (Click)
- Expansion of IRB Reliance Agreements

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Problem: Too many members, too few MDs, too few qualified reviewers

- FY 2012
  - 3 IRBs + Rapid Action IRB
  - Hard to get enough MDs to a meeting
  - Many reviewers inexperienced clinical researchers
  - Responses to stipulations reviewed by same IRB
- FY 2013
  - 1 IRB + Rapid Action IRB

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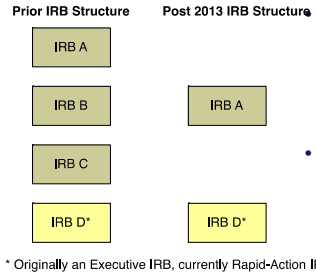
CHOP IRB Revised Structure



* Originally an Executive IRB, currently Rapid-Action IRB

- FY 2012
  - 3 IRBs – 17 members, 8 or 9 MDs
  - Each IRB met monthly – 3 total meetings
- FY 2013
  - 1 IRB – 11 members with 11 alternates
  - Meets 2x per month

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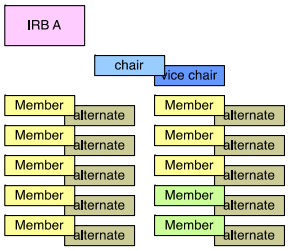
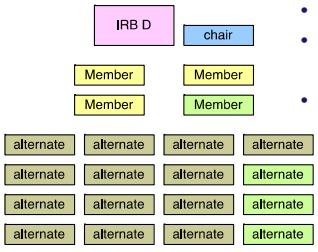
Post-2013 IRB A Structure



- 11 members – each with an alternate
  - member + alternate minimum: 20 of 24 meetings
  - 10% salary support CHOP members
  - Unaffiliated members receive fixed stipend
  - 2 unaffiliated members (green)

IRB D: Rapid Action IRB

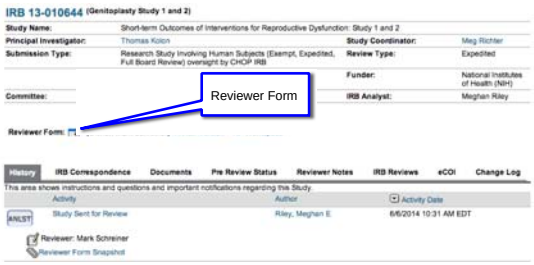


- No change in IRB D
- 5 members
  - all members of IRB A
- Meets only as needed
  - 4 – 6 times/year for
  - Emergencies
  - Urgent protocols
  - Decompress crowded agenda

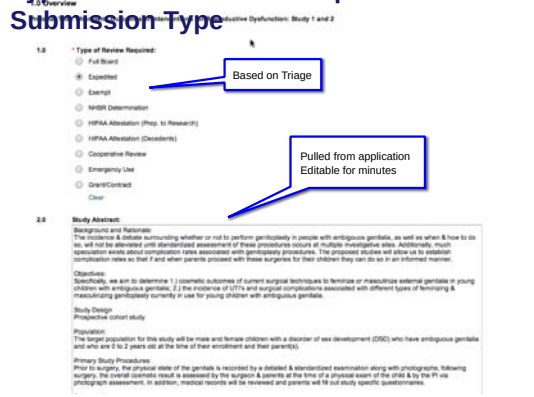
Integrating Reviewer Comments into eIRB (Click Commerce)

- Built in capability: Reviewer comments - embed on a smartform page or document attachment
  - Smartform comments relate to a page of the application (little value to CHOP IRB)
  - Attachments involve use of MS Word forms
- Programmers developed a “project type” to create a reviewer form

Reviewer Form



Type of Reviewer Form Depends on Submission Type



Reviewer Form Covers all Required Determinations

2.0 Criteria for Approval under [45 CFR 46.111(a) or 21 CFR 56] and CHOP Research Policies

Protocol Title: Short-term Outcomes of Interventions for Reproductive Dysfunction: Study 1 and 2

VIEW4F3E8C

1.0 **The risks to subjects minimized by using sound research design.**
(•) Yes ( ) No Clear

2.0 **Subjects are not unnecessarily exposed to risk.**
(•) Yes ( ) No Clear

3.0 **Whenever appropriate, procedures are combined with those already being performed for diagnostic or treatment purposes.**
(•) Yes
( ) No
( ) N/A
Clear

4.0 **Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be reasonably expected to result.**
(•) Yes ( ) No Clear

5.0 **Selection of subjects is equitable.**
(•) Yes ( ) No Clear

Comment Boxes are Interspersed

Children

19.0a * **Select the Subpart D categories that apply to this research. (Check all that apply)**
- [x] Minimal Risk (§46.404 or §50.51)
- [ ] Greater than Minimal Risk but prospect for direct benefit (§46.405 or §50.52)
- [ ] Greater than Minimal Risk, no prospect for direct benefit but yielding generalizable knowledge about the subjects disorder or condition (§46.406 or §50.53).
- [ ] Research not otherwise approvable, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (§46.407 or §50.54)
- [ ] Not able to determine

19.1 **Comments:**

Q15.0: Although the multi-center protocol references recruiting potential subjects over the phone, CHOP will not engage in phone recruitment activities.

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Required Modifications

- Stipulation section
  - protocol, consent form, application and other
- For full board studies stipulations pulled into meeting minutes and letter to investigator

27.0 **Consent Stipulations**

() The IRB has edited the consent form. Please review the edits to confirm they are correct. Once finalized, attach tracked and clean (all changes accepted) versions to application Section 12.01 (2.0) using the "Upload revision" button. Please do not delete any documents currently attached.

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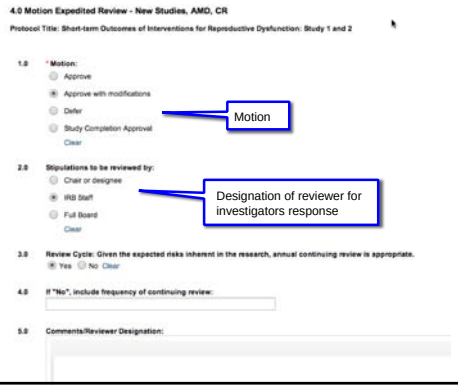
IRB Motion



4.0 Motion Expedited Review - New Studies, AMD, CR

Protocol Title: Short-term Outcomes of Interventions for Reproductive Dysfunction: Study 1 and 2

1.0 *Motion:
- Approve
- Approve with modifications
- Defer
- Study Completion Approval

Clear

Motion

2.0 Stipulations to be reviewed by:
- Chair or designee
- IRB Staff
- Full Board

Clear

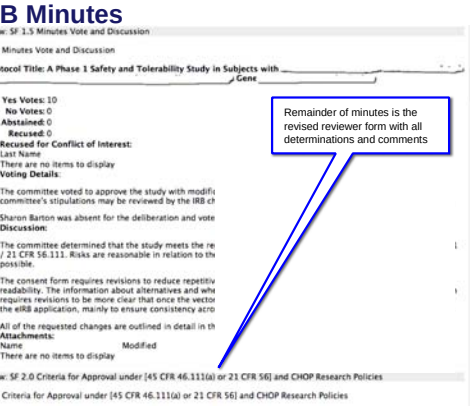
Designation of reviewer for investigators response

3.0 Review Cycle: Given the expected risks inherent in the research, annual continuing review is appropriate.
Yes No Clear

4.0 If "No", include frequency of continuing review:

5.0 Comments/Reviewer Designation:

IRB Minutes



View: SF 1.5 Minutes Vote and Discussion

1.5 Minutes Vote and Discussion

Protocol Title: A Phase 1 Safety and Tolerability Study in Subjects with [redacted] Gene [redacted]

Yes Votes: 10
1.0 No Votes: 0
Abstained: 0
Recused: 0
Recused for Conflict of Interest:
2.0 Last Name
There are no items to display
Voting Details:
3.0 The committee voted to approve the study with modifi committee's stipulations may be reviewed by the IRB ch

Sharon Barton was absent for the deliberation and vote
Discussion:

The committee determined that the study meets the re / 21 CFR 56.111. Risks are reasonable in relation to th possible.

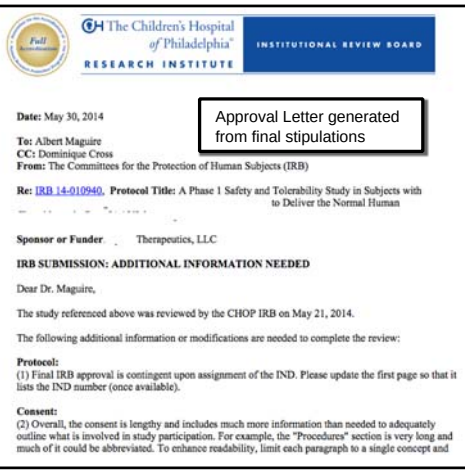
4.0 The consent form requires revisions to reduce repetitiv readability. The information about alternatives and wh requires revisions to be more clear that once the vecto the eIRB application, mainly to ensure consistency acro

All of the requested changes are outlined in detail in th
Attachments:
5.0 Name Modified
There are no items to display

Remainder of minutes is the revised reviewer form with all determinations and comments

View: SF 2.0 Criteria for Approval under [45 CFR 46.111(a) or 21 CFR 56] and CHOP Research Policies

2.0 Criteria for Approval under [45 CFR 46.111(a) or 21 CFR 56] and CHOP Research Policies



The Children's Hospital of Philadelphia RESEARCH INSTITUTE — INSTITUTIONAL REVIEW BOARD

Date: May 30, 2014

To: Albert Maguire
CC: Dominique Cross
From: The Committees for the Protection of Human Subjects (IRB)

Re: IRB 14-010940, **Protocol Title:** A Phase 1 Safety and Tolerability Study in Subjects with [redacted] to Deliver the Normal Human [redacted]

Sponsor or Funder [redacted] Therapeutics, LLC

IRB SUBMISSION: ADDITIONAL INFORMATION NEEDED

Dear Dr. Maguire,

The study referenced above was reviewed by the CHOP IRB on May 21, 2014.

The following additional information or modifications are needed to complete the review:

Protocol:
(1) Final IRB approval is contingent upon assignment of the IND. Please update the first page so that it lists the IND number (once available).

Consent:
(2) Overall, the consent is lengthy and includes much more information than needed to adequately outline what is involved in study participation. For example, the "Procedures" section is very long and much of it could be abbreviated. To enhance readability, limit each paragraph to a single concept and

Approval Letter generated from final stipulations

IRB Reliance Agreements

- Longstanding agreements
  - U Penn (2005), NCI PCIRB (2006), NCS (2010)
- Recent and in process agreements
  - Utah (Pediatric Critical Care), CHB-CCHMC-CHOP
  - PEDSnet (in process)
- Requirements
  - Must assume full responsibilities – we will no longer enter into facilitated reviews

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IRB Improvement Project

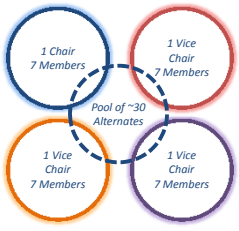
Michele D. Kipke, PhD, Vice Chair of Research

Targets for Intervention

1. Implement a Flexible IRB Model
2. Work with HSPP staff to streamline IRB pre-review and submission
3. Ongoing monitoring of performance indicators

New IRB Flexible Model

New IRB Model:



New IRB Leadership:

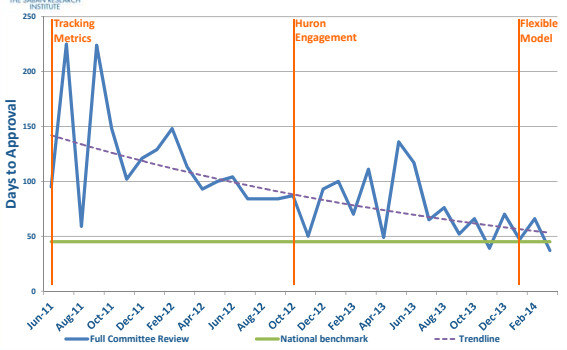
Alan Lewis, MD
Chair

Rob Bart, MD
Vice Chair

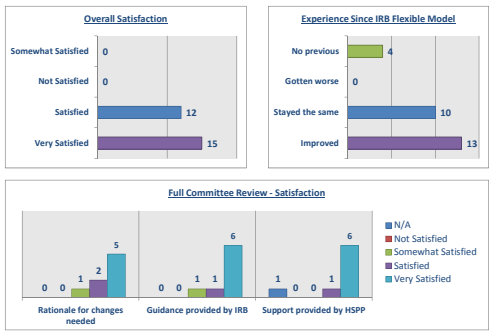
Girish Dhall, MD
Vice Chair

Jeff Gold, PhD
Vice Chair

IRB Turn Around Time



IRB User Satisfaction (Feb-April 2014)



IRB/Regulatory Support Specialist

- IRB application preparation and submission
- Regulatory and compliance documentation and submission to study sponsors
- Education and training of study teams regarding regulatory issues
- Liaison between the study team and the IRB

Flexibility Network Call
June 12, 2014

Increasing efficiency, quality, and satisfaction with more boards and meetings

Joseph Andrews, Jr.
Wake Forest School of Medicine
jandrews@wakehealth.edu
336-758-7658

The Issue with Full Board Review

- Turnaround Time
- Large agendas / Long meetings
- Large quorum requirements
- Long waits for re-review of tabled studies
- High volume of correspondence from IRB staff to investigators after monthly meeting
- Challenges IRB staff, investigators, and sponsors

WFSOM Background - July 2011

- Around 2400 active studies
- WFSOM average IRB-only turnaround time 46 days (33 IRB + 13 investigator)
- National Average 46 days (AAHRPP Metrics Survey Results for 2011)
- 4 IRB panels (each meeting once per month)
- About 18 regular members per panel
- 16 to 25 items per agenda

WFSOM Background Cont.

- Each IRB meeting took several hours
- Food breaks helped to refocus attention
- Quorum was often hard to achieve
  - Members needed to be late
  - Members needed to leave early
  - Agenda was juggled to accommodate needs
- Best discussion of submissions seemed to occur in the first hour or so

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The Idea for a Revised Process

- Examined the processes of highly efficient IRBs
- OHRP training video “Institutional Review Board (IRB) Membership” http://www.hhs.gov/ohrp/education/training/ded_video.html
- Ideal agenda size
- Times of day for meetings

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New Process Proposal

- Greater number of Boards with more frequent meetings
- 10-12 members per board
- 4-6 agenda items
- Midday meetings so members can use lunch time

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Our Analysis

- More than one meeting per month may be difficult to schedule
  - The shorter meetings should be easier to attend and take away less clinical time
- Smaller IRB panels may have inadequate expertise
  - Strategic assignment, use of alternates and consultants will eliminate this issue
- The workload may be overwhelming to IRB staff
  - Each week an analyst has only a few full board studies to handle
- Individual members may have to review more
  - Work is now spread between 16 meetings instead of 4

The Specific Changes

- Split each IRB panel into two (4 to 8)
- Rescheduled meetings so that each of the 8 panels meets every other week
- Boards 1-4 meet one week
- Boards 5-8 meet the next week
- Each month there are at least 16 IRB meetings

The Specific Changes Cont.

- Added members where necessary to each board
  - Some who left because of time conflict returned to try the new schedule
- Moved to a more convenient conference room with video & teleconferencing capabilities
  - We could use it now because of the smaller roster
- Assign Studies Strategically to the correct Board with appropriate expertise

Outcomes

- Andrews, J., Moore, J. B., Means, P., & Weinberg, R. B. (2012). An IRB transformation: Increasing quality and efficiency using existing resources. Journal of Research Administration, 43(2), 69-81
- IRB-Only Time
- 46 days total before change
- 21 days total afterwards (7 IRB + 14 investigator)

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Outcomes Cont.

- IRB meetings last about an hour
- Tabled protocols can be reconsidered in two weeks
- IRB members can return to their clinic or office for afternoon appointments
- Post-meeting correspondence can be sent same-day
- Minutes for meetings can be written up much more quickly

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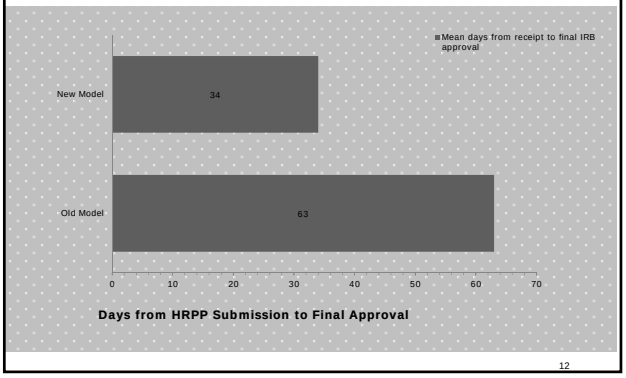
Overall HRPP Turn-around Time



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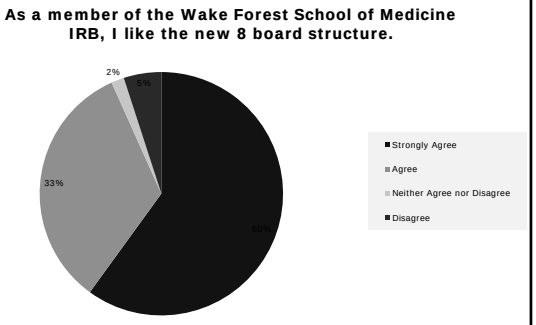
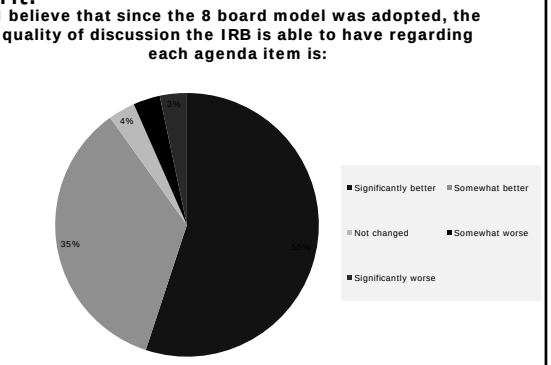
Outcomes Cont.

- IRB turnaround decreased 54%
- HRPP turnaround deceased 46%
- Discussion Time increased 33% per agenda item
- Smaller agendas increased the likelihood of thorough review of ALL submissions by ALL IRB members, not just primary reviewers

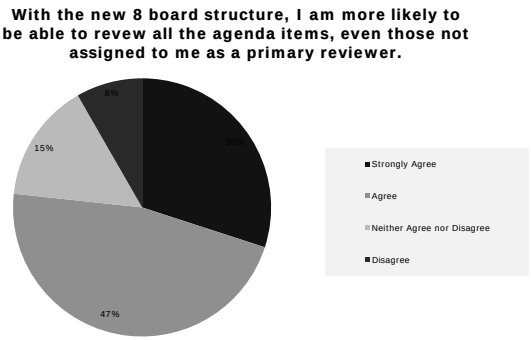
IRB Member Reaction 2012



IRB Member Reaction 2012 Cont.



IRB Member Reaction 2012 Cont.



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Sustainability

- July 2013 – February 2014
- Total HRPP turnaround 35 Days (15 HRPP / 20 Investigator)

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Sustainability Cont.

2013 IRB Member Survey

- Please describe your thoughts on the current duration of IRB meetings.
  - Too Short
  - About Right 100%
  - Too Long
  - No opinion

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Sustainability Cont.

2013 IRB Member Survey

- Please describe your thoughts on the time reviewers spend discussing protocols.
  - Too Short
  - About Right 100%
  - Too Long
  - No opinion

Sustainability Cont.

2013 IRB Member Survey

- indicate the percentage of scheduled board meetings that you attended within the past year.
  - 0-25%
  - 26-50%
  - 51-75% 3%
  - 76-100% 97%