Leading the way: The National Cancer Institute’s (NCI) Central Institutional Review Board (CIRB) for multi-site research

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National Cancer Institute

Presentation to Clinical Trials and Translational Research Advisory Committee (CTAC)
July 12, 2017
Special Call-Out to CIRB Colleagues

- EMMES Corporation
  - Brian Campbell
  - Laura Covington

- Westat
  - Martha Hering

- NCI
  - Jeff Abrams
  - Meg Mooney
  - Catasha Davis
  - Grace Mishkin
  - Jaci Goldberg
  - Linda Parreco
  - Lori Minasian
IRB Environment

Requires a single IRB of record:

- All non-exempt human subjects research protocols funded by the NIH that are carried out at more than one site in the United States
- **Effective Date:** January 25, 2018

Goal:

- Enhance and streamline the IRB review process in the context of multi-site research
- Eliminate duplicative IRB reviews & reduce unnecessary administrative burdens and systemic inefficiencies
- Without diminishing human subjects protections
Reactions to NIH Policy (Public Comments)

- **Support** among individual researchers, scientific and professional societies, and patient advocacy organizations
  - Believe it will streamline processes and enhance protections
- **Concerns** among academic institutions, IRBs and organizations:
  - Decreased quality and expertise of reviews
  - Difficult for sites to coordinate multiple single IRBs
  - Reluctance by PIs to participate in rigorous, multi-site research
  - Loss of local context influence

- **Call for data** that can provide insights into the adoption and experiences using a single IRB for multisite trials
NCI’s Central IRB

“Facilitated Review” model (2001-2012)

- Partnership between local institutions’ IRBs and NCI’s CIRB
- CIRB approved protocol, local IRBs reviewed for local context concerns
  - If none, they accepted CIRB as IRB of record
- Adoption of CIRB had stalled at ~45% of sites by 2011

“Independent” model (2013-present)

- CIRB is sole IRB of record, responsible for the local context considerations of each participating institution
  - No local IRB involvement
- Accredited in December, 2012 by Association for the Accreditation of Human Research Protection Programs (AAHRPP)
  - Formally launched in January, 2013
So how are we doing?

NCI CIRB Independent Model
Methods

- Review of key CIRB processes
- Analyze trial and site data from 2013-2016 for four NCI Networks*
  1. NCI National Clinical Trials Network (NCTN)
  2. NCI Experimental Therapeutics Clinical Trials Network (ETCTN)
  3. NCI Community Oncology Research Program (NCORP)
  4. Phase 0/I/II Cancer Prevention Clinical Trials Program (Consortia)

* There are a limited number of trials in these networks not covered by the CIRB; these have been excluded from the analysis
CIRB Processes
## NCI CIRB – Now has 4 Boards

<table>
<thead>
<tr>
<th>NCI CIRB Boards</th>
<th>NCI Division</th>
<th>Year Established</th>
<th>Frequency of Meeting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Late Phase</td>
<td>DCTD</td>
<td>2001</td>
<td>2x month</td>
</tr>
<tr>
<td>Pediatric</td>
<td>DCTD</td>
<td>2004</td>
<td>1x month</td>
</tr>
<tr>
<td>Adult Early Phase</td>
<td>DCTD</td>
<td>2013</td>
<td>2x month</td>
</tr>
<tr>
<td>Cancer Prevention and Control (CPC)</td>
<td>DCP</td>
<td>2015</td>
<td>1x month</td>
</tr>
</tbody>
</table>

DCTD: Division of Cancer Treatment and Diagnosis  
DCP: Division of Cancer Prevention
Ensuring High Quality Reviews

1. Wide representation of national oncology expertise and knowledgeable lay members on each Board
   - Ethicists, Nurses, Patient Advocates, Pharmacists, Physicians, and Statisticians
   - Assigned to reviews based on appropriate expertise and perspective
   - Collect Conflict of Interest Screening Worksheets from potential members
   - Undergo orientation and training

2. AAHRPP re-accreditation in 2015

3. Routine FDA inspection in 2015, resulting in no findings
Addressing Local Context

- Local context is addressed through series of worksheets
  1. Annual Signatory Institution Worksheet
  2. Annual Principal Investigator Worksheet
  3. Study-Specific Worksheet
  4. Worksheet to report potential unanticipated problems or noncompliance

- Information collected includes:
  - State and local laws
  - Conflict of Interest policy and management plans
  - Institutions’ boilerplate language for consent forms
  - Descriptions of study participant and vulnerable populations, including pregnancy, non-English language, etc.
Sophisticated Communications and Transparency

1. Use an online system (IRBManager) to share information among its Board members, sites, and Operations Office.
   - Provides seamless access to all CIRB-related information
   - Password protected
   - Integrated with multiple other NCI clinical trial systems

2. CIRB website ([www.ncicirb.org](http://www.ncicirb.org)) (newly revised)
   - Provides information for all CIRB stakeholders
   - Helpdesk for questions
   - Post minutes from each convened IRB review

3. Offer periodic Webinar educational seminars
CIRB Usage Data
2013-2016
Enrollment Across NCI Sites

By 2017, 81% of all unique institutions in the NCI system were enrolled in the CIRB (N=2228)
Number of CIRB Covered Studies (across all Boards), by Year

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>In Initial Review</td>
<td>12</td>
<td>13</td>
<td>24</td>
<td>25</td>
</tr>
<tr>
<td>Active Studies</td>
<td>255</td>
<td>391</td>
<td>341</td>
<td>404</td>
</tr>
<tr>
<td>Completed/Withdrawn</td>
<td>86</td>
<td>93</td>
<td>104</td>
<td>109</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>353</td>
<td>497</td>
<td>469</td>
<td>538</td>
</tr>
</tbody>
</table>

There is a 52% increase in the number of CIRB covered studies from 2013 to 2017.
## Completed Initial Study Reviews, by Year and Board

<table>
<thead>
<tr>
<th>Board</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>Median Days from complete Submission to Approval (2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult-Late Phase</td>
<td>11</td>
<td>13</td>
<td>18</td>
<td>18</td>
<td>39 days</td>
</tr>
<tr>
<td>Adult Early Phase</td>
<td>1</td>
<td>12</td>
<td>20</td>
<td>17</td>
<td>54 days</td>
</tr>
<tr>
<td>Pediatric</td>
<td>4</td>
<td>10</td>
<td>11</td>
<td>8</td>
<td>48 days</td>
</tr>
<tr>
<td>CPC</td>
<td>n/a</td>
<td>n/a</td>
<td>13</td>
<td>13</td>
<td>87 days</td>
</tr>
</tbody>
</table>
### Other Board Review Activities, in 2016

<table>
<thead>
<tr>
<th>Board</th>
<th>Continuing Reviews</th>
<th>Amendment Review</th>
<th>Expedited Reviews</th>
<th>Acknowledgements</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Late Phase</td>
<td>128</td>
<td>14</td>
<td>389</td>
<td>177</td>
<td>708</td>
</tr>
<tr>
<td>Adult Early Phase</td>
<td>46</td>
<td>9</td>
<td>205</td>
<td>102</td>
<td>363</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>55</td>
<td>24</td>
<td>144</td>
<td>208</td>
<td>432</td>
</tr>
<tr>
<td>CPC</td>
<td>10</td>
<td>7</td>
<td>49</td>
<td>19</td>
<td>87</td>
</tr>
</tbody>
</table>

In addition to initial reviews, Boards participate in several other IRB-related activities.
Initial Activation of CIRB Studies

Initial Site Activation of CIRB Studies using the CIRB vs. Local IRB (2013-2016)

By 2017, 96% of all initial studies activated at sites were through the CIRB
# Local IRB Response Time -- Major Protocol Amendments

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Total # Sites</th>
<th>Number of local-IRB Sites</th>
<th>Average Days to Reopen via local IRBs</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSABP-B-55</td>
<td>874</td>
<td>50</td>
<td>17.8</td>
</tr>
<tr>
<td>E1A11</td>
<td>492</td>
<td>138</td>
<td>26.5</td>
</tr>
<tr>
<td>GOG-0281</td>
<td>348</td>
<td>34</td>
<td>30.0</td>
</tr>
<tr>
<td>S1203</td>
<td>345</td>
<td>82</td>
<td>33.7</td>
</tr>
<tr>
<td>E1912</td>
<td>766</td>
<td>84</td>
<td>34.5</td>
</tr>
<tr>
<td>RTOG-1112</td>
<td>122</td>
<td>57</td>
<td>37.2</td>
</tr>
<tr>
<td>E1910</td>
<td>318</td>
<td>58</td>
<td>53.5</td>
</tr>
<tr>
<td>S1400</td>
<td>919</td>
<td>122</td>
<td>72.8</td>
</tr>
</tbody>
</table>

**Key advantage**: CIRB sites can implement amendment changes within 24-48 hours vs. local IRBs that take between 18-73 days.
CIRB Helpdesk Tickets

<table>
<thead>
<tr>
<th>Year</th>
<th>Total Helpdesk Tickets</th>
<th>Average Time to Resolution, in Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>6227</td>
<td>2.2 days</td>
</tr>
<tr>
<td>2014</td>
<td>6913</td>
<td>3.1 days</td>
</tr>
<tr>
<td>2015</td>
<td>6253</td>
<td>3.8 days</td>
</tr>
<tr>
<td>2016</td>
<td>6819</td>
<td>5.8 days</td>
</tr>
</tbody>
</table>

Top 5 Reasons for Contacting CIRB Helpdesk, 2016

<table>
<thead>
<tr>
<th>Category</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local context review process</td>
<td>3414</td>
</tr>
<tr>
<td>Personnel updates</td>
<td>1475</td>
</tr>
<tr>
<td>Current board reviews</td>
<td>978</td>
</tr>
<tr>
<td>CIRB procedures</td>
<td>267</td>
</tr>
<tr>
<td>Document search</td>
<td>140</td>
</tr>
</tbody>
</table>
Member Satisfaction of CIRB

**NCTN Satisfaction Survey** (online, December, 2016, N=268)

- 84% indicated that the CIRB “met” or “exceeded” their expectations
  - 14% indicated CIRB “does not meet expectations—needs some improvement”; 2% indicated “needs significant improvement”
  - Respondents: key Group personnel and leadership

**ETCTN Satisfaction Survey** (online, April, 2017, N=280)

- **Satisfaction scale**: 1 (not at all satisfied) to 5 (very satisfied)
  - PIs: 56% reported score of 4 or 5; mean=3.6
  - Staff: 58% reported score of 4 or 5; mean=3.7
  - Respondents: Grant PIs and Site Staff

Overall satisfaction of CIRB is high within 2 major CTEP networks
Summary
Lessons Learned -- CIRBs

- Require a commitment of resources (contracts, staffing, Boards)
- Require carefully developed processes to manage local context issues, timelines, and conflicts of interest
- Require ongoing quality controls – e.g., accreditation
- Must have the ability to communicate easily with multiple stakeholders (PIs, local institutions, Board members, clinical performance sites)
  - Website
  - Help Desk
  - IT systems
- Widespread adoption and high satisfaction is achievable at a national level
Questions?
Sites “Not Enrolled” (N=413 through 2016)

<table>
<thead>
<tr>
<th>Sites Not Enrolled (N = 413; 19%)</th>
<th>% of Total Not Enrolled</th>
<th>Average Total Accruals 1/1/2013 – 7/31/2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>236</td>
<td>56%</td>
<td>0</td>
</tr>
<tr>
<td>68</td>
<td>16%</td>
<td>1 to 5</td>
</tr>
<tr>
<td>86</td>
<td>21%</td>
<td>5 to 8</td>
</tr>
<tr>
<td>29</td>
<td>7%</td>
<td>8 or more</td>
</tr>
</tbody>
</table>

Over half of sites not enrolled in CIRB have had “0” accruals since 2013
Helpdesk -- Satisfaction with Ticket Response

Reported Satisfaction with Helpdesk Interaction, 2016*

- Response time to inquiry (N=873): 82% Not Satisfied, 14% Satisfied, 4% Very Satisfied
- Completeness of response (n=857): 82% Not Satisfied, 14% Satisfied, 4% Very Satisfied
- Overall Helpdesk interaction (N=869): 83% Not Satisfied, 13% Satisfied, 4% Very Satisfied

Of those responding, satisfaction is high for Helpdesk performance

*13% response rate