Bottlenecks of Study Start Up & Some Suggestions for Efficiencies

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Special Thanks...

The Clinical Trials Transformation Initiative (CTTI)

- A public/private partnership between the FDA and Duke (with much industry representations)
- Robert Califf, MD - Duke
- Briggs Morrison, MD - Astra Zeneca (Pfizer)
- Diana Abbott, PhD - Duke
- Jean Bolte RN – Duke
- And so many more!
Reasons for the Study

- Establish a baseline of actual time spent during various phases of the start up period

- Create effective approaches for improving the start up phase
  - Providing “norm” to those who want to benchmark against industry standards
  - The development of standard terms
  - Time points to be collected moving forward
Collaboration At It’s Best

19 CTTI member organizations submitted retrospective data on site/study information between January 1, 2009 and January 1, 2010

- 2 academic
- 4 ARO/CRO
- 2 biotechnology
- 2 medical device
- 1 government
- 2 Investigator
- 6 pharmaceutical
What Was Collected

- Unique identifier as per their system
- Protocol ID
- Site type
- IRB type
- Therapeutic area
- Sponsor name
- The date the protocol was sent by the sponsor/CRO to the site
- The date the protocol was received by the site
- The date the protocol was submitted to the IRB
- The date of the IRB’s final decision on the protocol
- The date the contract was executed
- The date the first patient was enrolled at that site
The Data Flowed In

- 10,673 lines of original data were received
- 5,396 lines of data (50.6%) were used
  - 64% Pharmaceutical companies
  - 13% ACRs/CROs
  - 10% Academic organizations
  - 10% Biotechnology
  - 3% Others
The Sites Represented

- 25.6% Academics
- 24.6% Private practices
- 6.6% Hospital-based
- 3.1% VA
- 39.2% Unknown
Therapeutic Representation

- 20.7% Hematology
- 19.1% Cardiovascular/metabolic
- 14.1% Other
- 13.4% Neurosciences
- 8.9% Allergy/respiratory
- 4.7% Pain
- 4.6% Inflammation
Some Realities Learned Early On

- Little standardization for what is collected
- Little standardization for what it’s called
- Multiples places where it’s stored
What Was Measured

The date the protocol was sent by the sponsor/CRO to the site against...

1. The date the protocol was received by the site
2. The date the protocol was submitted to the IRB
3. The date of the IRB’s final decision on the protocol
4. The date the contract was executed
5. The date the first patient was enrolled at that site

*If absolute dates were not available, approximate dates were provided
*US sites only, Phase 2-4 multicenter trials
If You had to choose one factor that would be the strongest predictor of how long it will take a site to get up and going what would it be?
#1 - The Type of IRB Used

- Or maybe...
  - Is it really more about the **type of the sites and studies** that must utilize a local IRB and all that entails
# IRB Process

<table>
<thead>
<tr>
<th>Event</th>
<th>Median Time (days)</th>
<th>Significantly higher than median time (days)</th>
<th>Type of site higher than median site</th>
<th>Significantly lower than median time (days)</th>
<th>Type of site lower than the median site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of days between date protocol was received at site and date of protocol submission to IRB</td>
<td>44</td>
<td>51 66 68</td>
<td>VA Academic hospital-based</td>
<td>30 39</td>
<td>private practice independent sites</td>
</tr>
<tr>
<td>Number of days between IRB submission and IRB final decision</td>
<td>9</td>
<td>17 33 55</td>
<td>academic hospital-based VA</td>
<td>6 10</td>
<td>private practice independent</td>
</tr>
<tr>
<td>Central IRB decision</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local IRB decision</td>
<td>35</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Then There’s The Lawyers

<table>
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<tr>
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<th>Significantly lower than median time (days)</th>
<th>Type of site lower than the median site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of days between date protocol is received at site and date of contract execution</td>
<td>54</td>
<td>57 74 102 104</td>
<td>Independent academic VA hospital-based</td>
<td>35</td>
<td>Private practices</td>
</tr>
</tbody>
</table>
The One Everyone Loves to Measure

<table>
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<tr>
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<th>Median Time (days)</th>
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<th>Type of site higher than median site</th>
<th>Significantly lower than median time (days)</th>
<th>Type of site lower than the median site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of days between IRB final decision and date of FPFV</td>
<td>80</td>
<td>89 102</td>
<td>Private practice hospital-based</td>
<td>70 72</td>
<td>VA &amp; independent Academic</td>
</tr>
<tr>
<td>Central IRB</td>
<td>74 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local IRB</td>
<td>95 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1\textsuperscript{st} subject consented within ...

- 30 days = 90+\% chance of success
- 60 days = 50\% of success
- 90 days = <10\% chance of success

Source: AAI Pharma 2005
Take Aways

- Data that does not reside in one central location within a company places a challenges upon anyone to measure and act upon it
- A lack of industry standards regarding the terms or milestones to measure creates continued inefficiencies
- The use of a central IRB results in the site’s approval 27 days sooner than a local IRB
- The site that uses a central IRB enrolls their first subject 21 days sooner than a site that uses a local IRB
- We’re not done...

Prospective study to follow
Thank You

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