A Case Study: Building a Research Program that Minimizes Legal Risk and Maximizes Compliance

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The Backdrop

- Common themes prevailed in AHCs
  - Clinical Research had questionable academic value
  - Variable appreciation for the distinction between clinical practice and clinical research
  - Variable appreciation for the rules of engagement
  - Compliance expectations were perceived by those in Academia to be lower than those expected in Pharma
  - Variable PI and staff expertise and limited resources
  - Limited investment in infrastructure to support the enterprise

What Changed?

- Clinical Trials a way to differentiate competition in the health care market place
- Early phase of drug development occurring in AHCs with greater frequency
- Rapid growth in investigator initiated research
  - Manufacturing occurring in academia
  - Increase in number and complexity of financial conflicts of interest
  - Increase in management of multisite clinical trials
Past vs Present: A Model of Integration/Collaboration

Strategic Plan: Potential for Innovation

The Challenges/Disincentives

- Culture - limited incentive for faculty to engage
- Administrative burden perceived to be inexorable
- Cumbersome approval processes
- Variously trained support staff with limited longevity
- Limited ability of community to leverage existing resources
- Funding for the support structure
- Interface of IT support systems
Recommendations of External Review

• Centralizing clinical research support services

• Adopting a service model for all functions that support principal investigators

• Investing in IT infrastructure to facilitate access to information and provide support tools that enable clinical research

• Establish a leadership position with accountable authority and responsibility to work across the institution to optimize clinical research standards at Penn Medicine

Evolution of Central Resources

Engaged Leadership and Implemented Oversight

Dean & EVP, PSOM
Vice Provost for research, University
Clinical Trials
- Human Data Sets
- Tissue/biospecimen
- Mechanistic or Physiologic study in human subjects
- Sociobehavioral
- Other
- Survey research
- Quality Improvement research
- Epidemiological research

Continued growth in clinical trial volume and complexity

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Protocols</th>
<th>Funding $</th>
</tr>
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<tbody>
<tr>
<td>2014</td>
<td>10,000</td>
<td>30,000,000</td>
</tr>
<tr>
<td>2015</td>
<td>20,000</td>
<td>50,000,000</td>
</tr>
<tr>
<td>2016</td>
<td>30,000</td>
<td>70,000,000</td>
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Growth in # of INDs

<table>
<thead>
<tr>
<th>Size of Site Relying on Penn IRB</th>
<th>Number of Protocols</th>
<th>Number of Studies with Penn Serving as IRB of Record for Other Sites</th>
</tr>
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<tbody>
<tr>
<td>&lt; 5 sites</td>
<td>81</td>
<td>17</td>
</tr>
<tr>
<td>5-10 sites</td>
<td>86</td>
<td>3</td>
</tr>
<tr>
<td>10-20 sites</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 20 sites</td>
<td>8</td>
<td>2</td>
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<tr>
<td>Total sites relying on Penn</td>
<td>278</td>
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Awareness of the Risk Proposition

- **Study Subject Harm**
- **Reputational Risk**
  - Patient harm
  - Ethical considerations
  - Conflict of Interest
  - Policy and regulatory compliance
- **Financial Liability**
  - Study subject, funding agency
Followed by

- An FDA inspection………..

Clinical trials are complex and highly regulated

Standards are set by federal (FDA, OHRP, NIH, CMS) or state regulations and institutional policies

Enabling Compliant Research – a shared responsibility
Clinical Trial Lifecycle – Where does the risk exist?

**Key Observations**

- Drug manufacturing and management of investigational products
- Academic Faculty serving as regulatory sponsors
- Oversight of clinical trial conduct – Monitoring and Auditing
- Education and retention of a trained workforce
- Prospective reimbursement analysis and its compliance oversight
- ClinicalTrials.gov reporting requirements
- Conflict of Interest

Another External Assessment...

- Organization and oversight
- Infrastructure (IT, space, personnel, and training)
- Clinical Trial review and approval process
- Conflict of interest policies
- Define metrics for tracking compliance goals
- Assess the need for ongoing external input
- Recommend the frequency of reports to Trustees
Key elements of an effective compliance program include:

- Establish standards and procedures to prevent and detect noncompliance.
- Exercise effective compliance oversight via engagement of multiple levels of management, including the board of directors, senior management and compliance personnel; organization's governing authority must be knowledgeable about the content and operation of the compliance program.
- Exercise due diligence to avoid delegation of authority to individuals with a history of behavior inconsistent with an effective compliance program.
- Communicate and educate employees on relevant standards and procedures and other aspects of the compliance program.
- Monitor and audit compliance programs, evaluate periodically for effectiveness, and have and publicize a system for employees and agents to report or seek guidance regarding noncompliance without fear of retaliation.
- Promote and consistently enforce the compliance program via incentives and disciplinary measures.
- Respond appropriately to noncompliance and take steps to avoid future noncompliance, including making any revisions to the compliance program.

Penn Medicine Compliance Program

Educating Research Professionals
Clinical Trials Risk Mitigation: Recommendations

<table>
<thead>
<tr>
<th>Standardization and Oversight</th>
<th>Status</th>
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<tbody>
<tr>
<td>Institute formal scientific reviews in Departments</td>
<td>☐</td>
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<tr>
<td>Increase consistency and transparency in COI policies and process</td>
<td>☐</td>
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<tr>
<td>Standardize process and coordinate oversight across Penn Med hospitals</td>
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<td>Bring Investigational Drug Service into compliance with &quot;Good Manufacturing Practices&quot;</td>
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<tr>
<td>Expand research compliance program</td>
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<tr>
<td>Centralize and audit prospective reimbursement analysis</td>
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<tr>
<td>Monitor compliance with clinicaltrials.gov</td>
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<tr>
<th>Training</th>
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<tr>
<td>Mandate training for investigators, sponsors, monitors</td>
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<td>Reduce coordinator turnover through career advancement and training</td>
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Three years later…. Improving… not there yet

The End Game

- Create a culture conducive to clinical research
- Demonstrate regulation and facilitation can coexist
- Enable entrepreneurial activity
- Create a workforce of skilled clinical and translational investigators
- Attract sponsors and commercial partners
- Measure impact