## 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

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## 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

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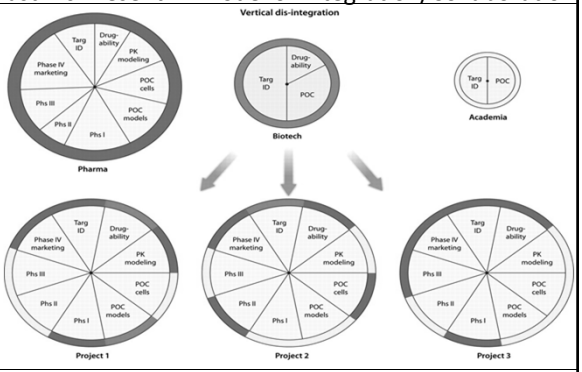
## Past V.s Present: A Model of Integration/Collaboration

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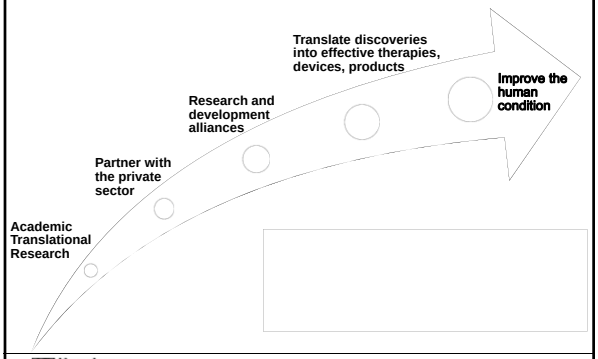
## Strategic Plan: Potential for Innovation

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## The Challenges/ Disincentives

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

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## 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

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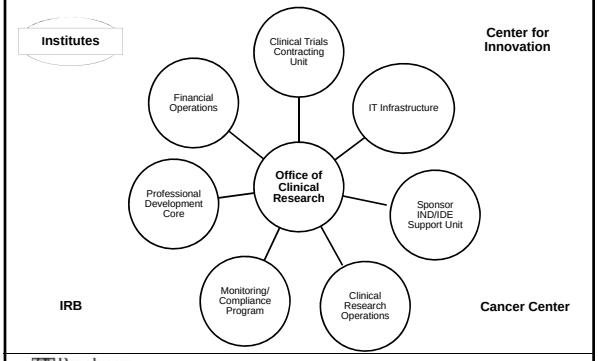
## Evolution of Central Resources

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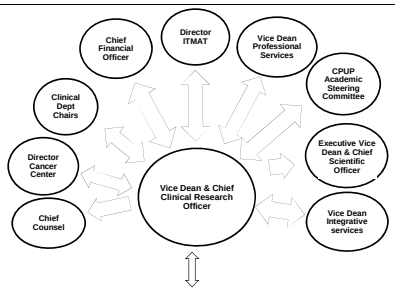
## Engaged Leadership and Implemented Oversight

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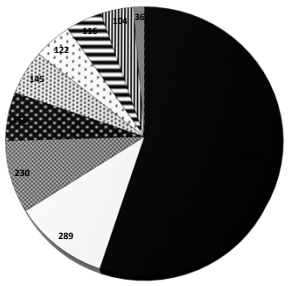
## Penn's Clinical Research Portfolio




- Clinical Trials
- Human Data Sets
- Tissue/biospecimen
- Mechanistic or Physiologic study in human subjects
- Sociobehavioral
- Other
- Survey research
- Quality Improvement research
- Epidemiological research

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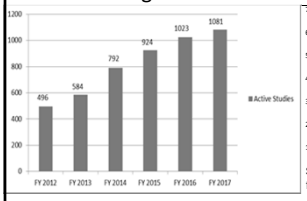
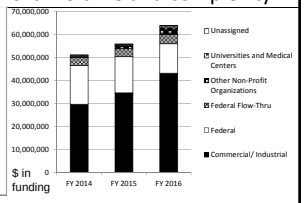
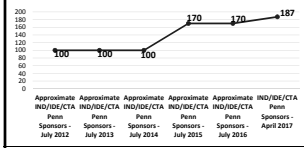
## Continued growth in clinical trial volume and complexity




Growth in # of INDs




| # of protocols with > 1 site relying on Penn IRB | |
|---|---|
| 1 -5 sites | 81 |
| 6-10 sites | 5 |
| 11-20 sites | 3 |
| 20-30 sites | 3 |
| # of active studies with Penn serving as IRB of record for other sites | 91 |
| Total # of additional sites relying on Penn | 278 |

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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

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## Followed by

- **An FDA inspection……..**

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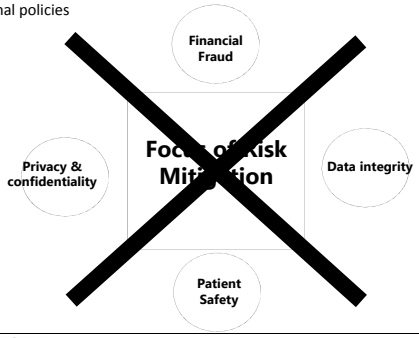
## Clinical trials are complex and highly regulated

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

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## Enabling Compliant Research – a shared responsibility


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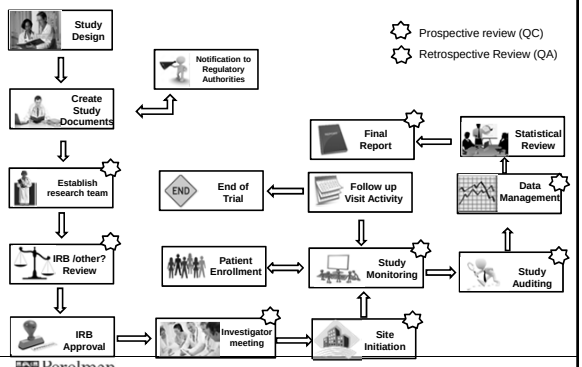
## Clinical Trial Lifecycle – Where does the risk exist?

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## 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

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## 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
- Clinical Trials.gov reporting requirements
- Conflict of Interest

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## 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.

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http://www.ussc.gov/guidelines/2015-guidelines-manual/archive/2014-chapter-8

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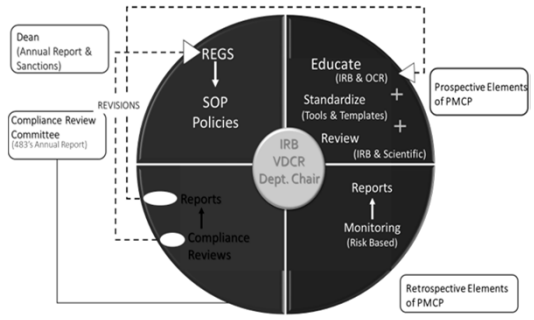
## Penn Medicine Compliance Program

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## Educating Research Professionals

CR 101

E learning Module

Access Training

**Entry Level**
**CRC A**

**Certificate Program**

**Early Career**
**CRC B/C**

**Masters**
**Reg Affairs**

**Mid Career**
CRC C
Project Managers
Reg Affairs specialist

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## Clinical Trials Risk Mitigation: Recommendations

| Standardization and Oversight | Status |
|---|---|
| • Institute formal scientific reviews in Departments | ○ |
| • Increase consistency and transparency in COI policies and process | ○ |
| • Standardize process and coordinate oversight across Penn Med hospitals | ○ |
| **Compliance** | |
| • Bring Investigational Drug Service into compliance with "Good Manufacturing Practices" | ○ |
| • Expand research compliance program | ○ |
| • Centralize and audit prospective reimbursement analysis | ○ |
| • Monitor compliance with clinicaltrials.gov | ○ |
| **Training** | |
| • Mandate training for investigators, sponsors, monitors | ○ |
| • Reduce coordinator turnover through career advancement and training | ○ |

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## Three years later…. Improving… not there yet


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## 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

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