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

Emma A. Meagher, MD
Vice Dean, Clinical Research
Senior Associate Vice Provost
University of Pennsylvania

Perelman School of Medicine
University of Pennsylvania

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

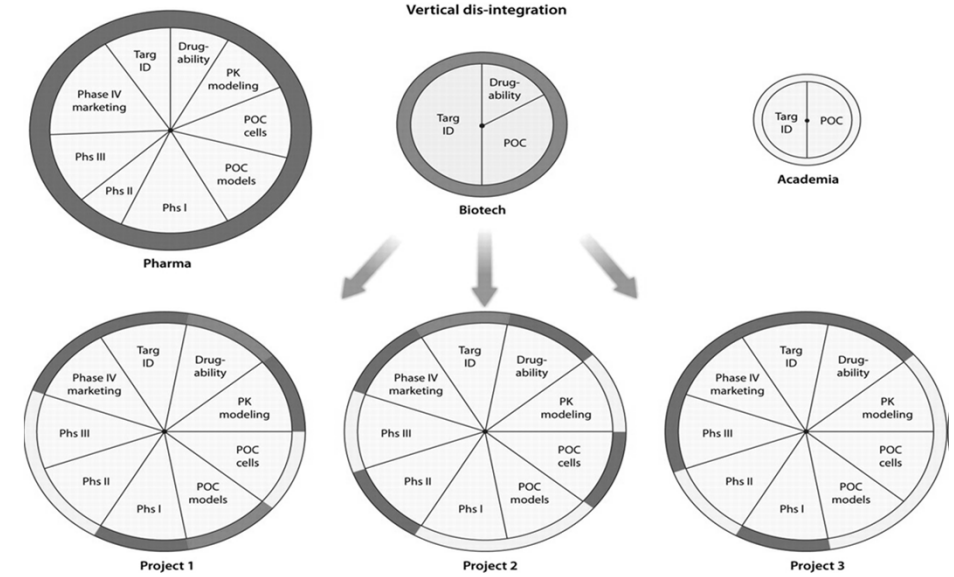
What Changed?

- 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

Perelman School of Medicine University of Pennsylvania

3

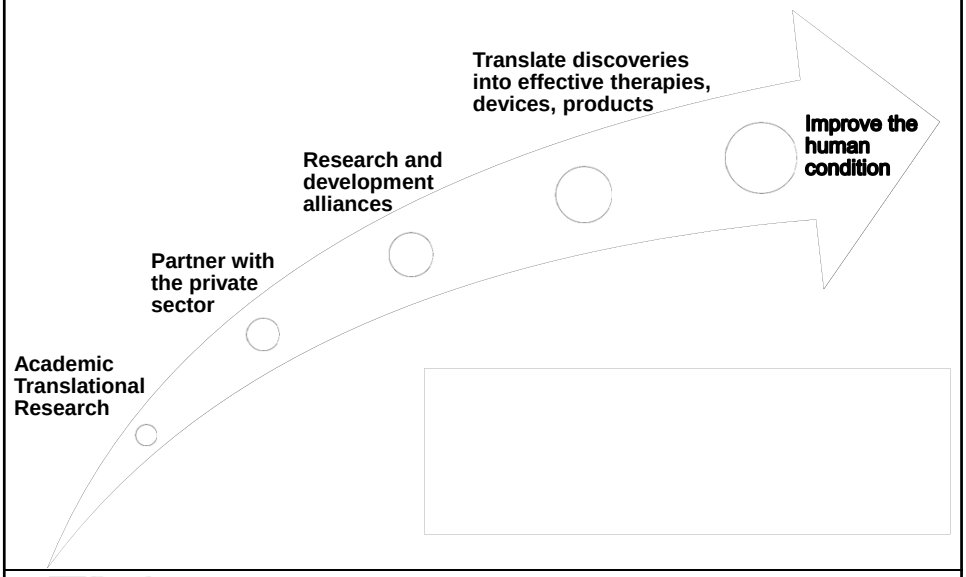
Past V.s Present: A Model of Integration/Collaboration



Perelman School of Medicine University of Pennsylvania

4

Strategic Plan: Potential for Innovation



Perelman School of Medicine University of Pennsylvania

5

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

Perelman School of Medicine University of Pennsylvania

6

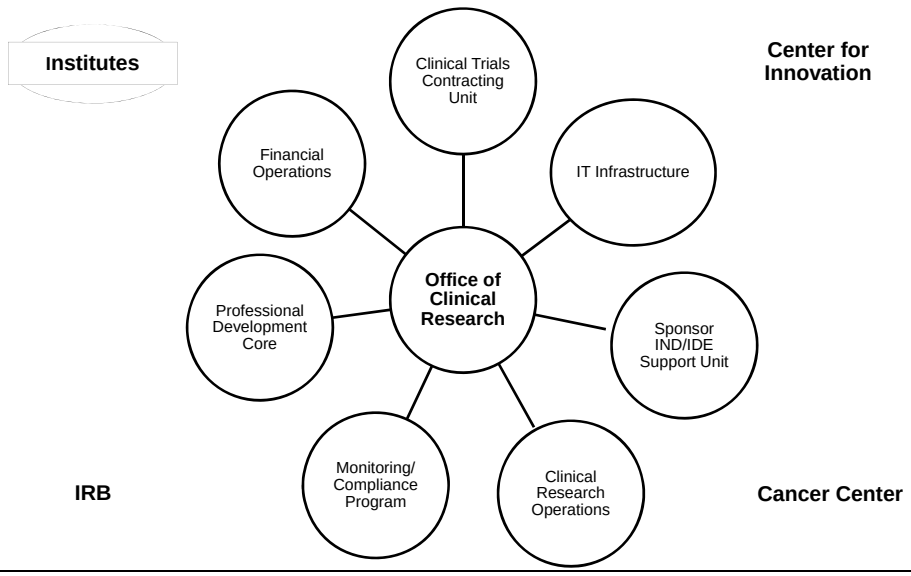
Recommendations of External Review

- 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

Perelman School of Medicine University of Pennsylvania

7

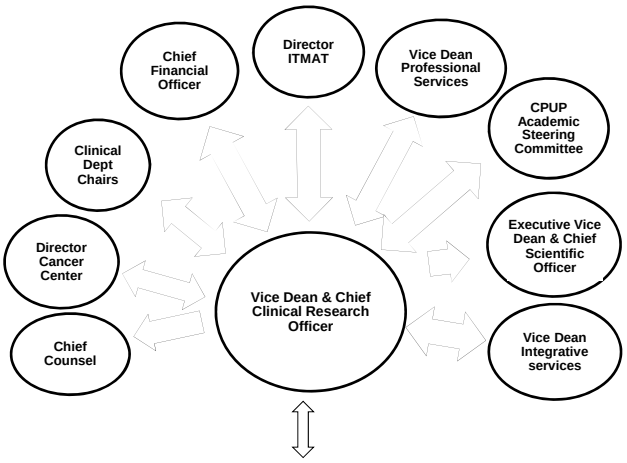
Evolution of Central Resources



Perelman School of Medicine University of Pennsylvania

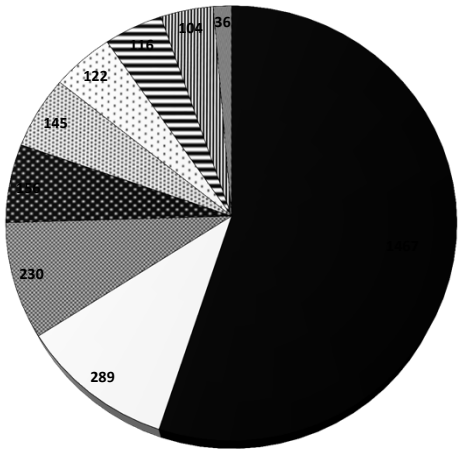
8

Engaged Leadership and Implemented Oversight



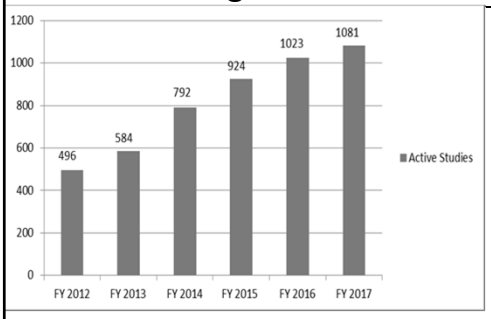
Dean & EVP, PSOM
Vice Provost for research, University

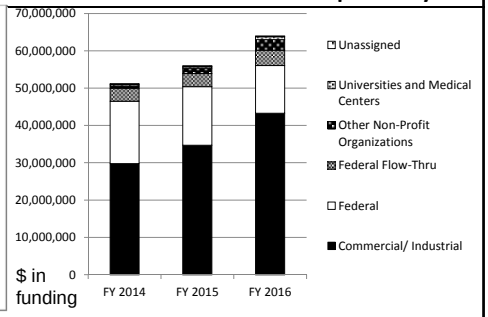
Penn's Clinical Research Portfolio



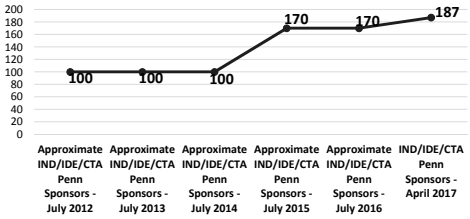
- Clinical Trials
- Human Data Sets
- Tissue/biospecimen
- Mechanistic or Physiologic study in human subjects
- Sociobehavioral
- Other
- Survey research
- Quality Improvement research
- Epidemiological research

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**

Perelman School of Medicine University of Pennsylvania

11

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

Perelman School of Medicine University of Pennsylvania

12

Followed by

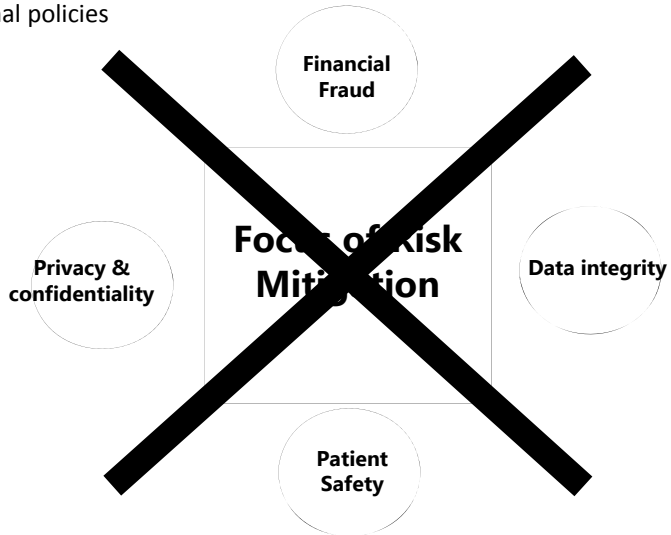
- **An FDA inspection…….**

Perelman School of Medicine University of Pennsylvania

13

Clinical trials are complex and highly regulated

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



Perelman School of Medicine University of Pennsylvania

9

14

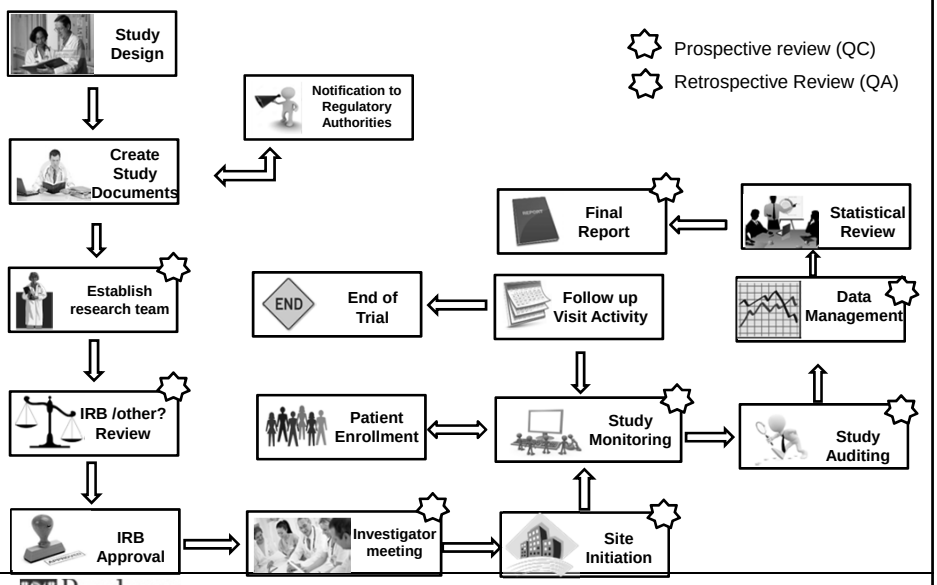
Enabling Compliant Research – a shared responsibility

Perelman School of Medicine University of Pennsylvania

6

15

Clinical Trial Lifecycle – Where does the risk exist?



Perelman School of Medicine University of Pennsylvania

16

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

Perelman School of Medicine University of Pennsylvania

17

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

Perelman School of Medicine University of Pennsylvania

14

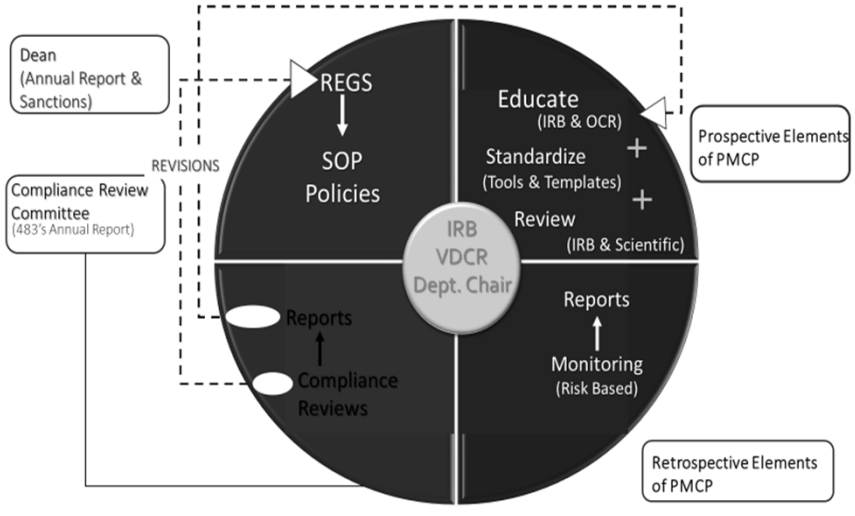
18

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.

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

Penn Medicine Compliance Program



Educating Research Professionals

CR 101

E learning Module

Access Training

Certificate Program

Masters Reg Affairs

Entry Level
CRC A

Early Career
CRC B/C

Mid Career
CRC C
Project Managers
Reg Affairs specialist

Perelman School of Medicine
University of Pennsylvania

21

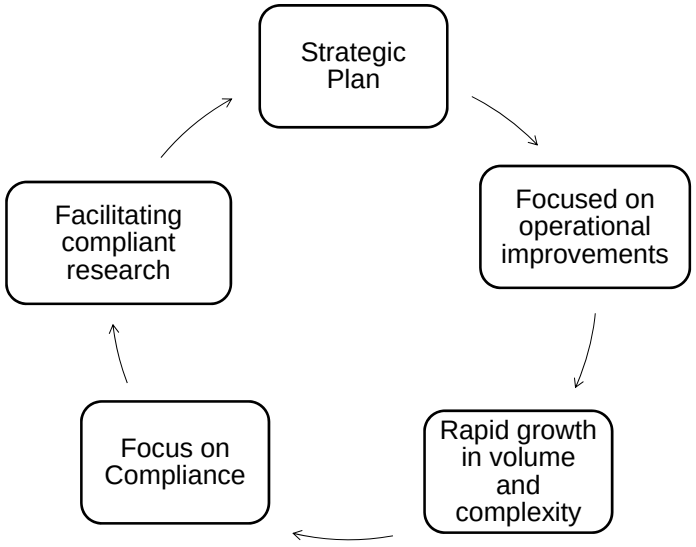
Clinical Trials Risk Mitigation: Recommendations

	Status
Standardization and Oversight	
• **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**	◯

Perelman School of Medicine
University of Pennsylvania

22

Three years later…. Improving… not there yet



Perelman School of Medicine University of Pennsylvania

8

23

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

Perelman School of Medicine University of Pennsylvania

24

Perelman School of Medicine
University of Pennsylvania

25