



Research and Compliance

Understanding the Risks in the Context of Both Large and Small Entities

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Presentation Objectives

- How research fits into compliance objectives.
- Issues that are driving the need for a Research Compliance Program.
- Underpinnings of a successful Research Compliance Program.
- Importance and roles of key stakeholders to research compliance.



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Overview of the Pressures

Volume of Activity	↑
Complexity	↑
Competition	↑
Scrutiny	↑
Demand for Accountability	↑
Large investments in facilities	↑
Pressure to maintain / reduce admin costs	↑
Funding levels	↔

During a time when many of these growth factors are occurring simultaneously, many organizations have failed to make an associated *and proportionate* investment in the compliance infrastructure necessary to keep risks in check.

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Who Applies the Pressure?

- What agencies are concerned with research compliance and what are the issues? (just a selection!)

Human Subject Protection

- OHRP
- FDA
- NIH

Clinical Research Billing

- CMS
- OIG
- DOJ
- State AG

Federal Grants

- NIH
- OIG
- DOJ

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How Did We Get Here? – Top Issues

1. Movement of clinical research into the community setting

- For many years, clinical research has been the domain of academic medical centers...not any more.
- Some estimates peg 40% of clinical research is performed at a community hospital or in independent physician practices.



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How Did We Get Here? – Top Issues

1. Clinical research into the community setting

Academic Medical Centers

- Focus on bench/basic and animal research
- Investigators hired and protected time granted for faculty to engage in research
- Research part of the mission
- Pre-award and post-award administrative infrastructure in place
- Executive-level leadership for research enterprise
- Sophisticated research accounting systems
- Prevalence of federally sponsored research
- Publication of findings is expected
- Perception (and reality) of more bureaucracy compromises timeliness

Community Hospitals

- Greater focus on clinical research
- Open medical staff vs. Closed med staff
- Few community health systems have protected time for clinicians to pursue research opportunities
- Organizational culture does not view research as a priority
- Limited administrative infrastructure
- Leadership for research programs are at the PI or the departmental level
- Focus is on CCOPs and industry sponsored research
- Less sophisticated approach to establishing the optimal portfolio of research to match strategic objectives

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Top Issues

2. Not knowing the studies conducted at your institution; not knowing who the patients are

- Seems like a simple thing, but it can be quite complicated.
- Who knows? The physician.
- Consider developing a process to be informed of the patient's enrollment at the time of signing informed consent
 - CTMS, secure email, or fax notification



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Top Issues

2. What is Going on Under My Roof?!

- Physicians may be signing Clinical Trial Agreements without hospital's involvement with the intention of performing most services in their private practice office.
- Once services associated with a clinical trial necessitate use of hospital resources (i.e., nurses, equipment, space), the hospital takes on risk.
 - Even if only Standard of Care services are involved in the trial's tests and procedures, there are responsibilities that need to be met
- Many organizations have developed policies that dictate the importance and requirements for clinicians to engage the hospital when/if its facilities may become necessary to execute the provisions of a clinical research protocol.

- Research feasibility.	- Identification of each research participant.
- Credentialing issues.	- Contract that details payment for non-SOC.
- Copy of IRB approval letter.	- Documentation that Medicare intermediary has provided approval, as necessary.

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Top Issues

3. Not knowing who got paid for what

- Items and services paid for by the sponsor cannot be billed to insurance
- Who are the parties to the clinical trial agreement?
- Who took the money? What is the money for?
- Is the hospital receiving money that must be paid to a physician?

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Top Issues

4. Stark Laws lurking in the confusion of documents

- Is the hospital taking money which must be paid to a physician?
(For example, professional fees for radiology services)
- A financial relationship between a hospital and a physician who refers Medicare patients to the hospital must meet a Stark exception (and Anti-kickback Statute compliance must also be considered)
- Is there a negotiated rate for the physician's charges?

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Top Issues

5. Abiding by the financial discussion in the research informed consent

- Anything promised free in the research informed consent cannot be billed to insurance.
- The informed consent must be written at a 6th to 8th grade reading level – it is interpreted from the perspective of the patient.
- What is being promised free in the informed consent? Is there a system to manage this information?

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Top Issues

6. Not having a process to review research-related claims before sending to third party payors

- Services which cannot be billed to insurance must have their charges directed to the study. There must be a process to:
 - A. Bring all the information together about the study to know which services can be billed to insurance and which can't ("Coverage Analysis"); and
 - B. Review claims against the Coverage Analysis.
- The information in a Coverage Analysis should be coordinated between the hospital and the physician.

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Top Issues

7. Auditing your IRB

- Do you know who your IRB is?
- An institution can outsource the IRB function, but it cannot outsource the liability.
- Compliance audits should occur for both internal IRBs and external IRBs.
- Write into your contract with an external IRB the ability to conduct compliance audits.



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Top Issues

8. Others

- Faculty start-ups
- Tech transfer
- Equity interests of institution
- International collaborations
- Sub-recipient monitoring
- Cost accounting standards
- Research misconduct
- Stem cells and other scientific controversy
- HIPAA / Privacy
- Investigator Salary and Effort



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Addressing the Issues

Competing / misaligned interests of key stakeholders

- Principal investigators (“PIs”)
- Research support (research asst., CRCs, RRNs, etc.)
- Students
- Board members
- Tax payers
- Institutional, Departmental, and Divisional administrators
- Federal agencies
- Commercial sponsors
- Suppliers and procurement specialists
- Foundations
- Donors and investors
- Human subjects
- Advocacy groups



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Addressing the Issues

Establishing a Research Compliance Program

- Oversight, management, and mitigation of the risks.
- Leadership and guidance for the various constituents and stakeholders with a role in preserving institutional integrity and compliance.
- Need for experts who understand that health care research is fundamentally different from other operational activities of a health care organization.
 - Activities “look” the same as other key practices and processes, but the nuance and dynamics are often mistaken or incorrectly applied.
 - This can exacerbate risks.



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Addressing the Issues

Establishing a Research Compliance Program

- It is imperative that organizations seeking to grow (or nurture) research, at a minimum, should have the following:
 1. **Sufficient compliance and administrative leadership over research**
 2. **Effective policies & SOPs**
 3. **Solid internal controls (both pre- and post-award)**
- The absence of such items may result in additional pressures and the realization of the risks referenced in this presentation.

Institutions that are “performance sites” for health care research need a research compliance program that can manage compliance risks, preserve regulatory integrity yet allow scientists to pursue innovative research opportunities that can lead to breakthroughs and advancements.

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Risks of Inaction

<p style="text-align: center;">Damage to One's Reputation</p> <ul style="list-style-type: none"> • No organization wants the negative publicity that can come from alleged wrongdoing. <ul style="list-style-type: none"> – Northwestern, Hopkins, & Harvard - effort – Penn - informed consent & COI – Mayo & Yale - cost transfers, effort, cost sharing – Rush - clinical trial billing – Vermont - research misconduct – U. of Oklahoma - informed consent 	<p style="text-align: center;">Regulatory Consequences</p> <ul style="list-style-type: none"> • CIAs or CCAs • Loss of letter of credit funding authorization • Suspension, debarment, and exclusion of individuals (or even entire programs or institutions) engaged in research • Additional monitoring
<p style="text-align: center;">Costly Operational Redesign</p> <ul style="list-style-type: none"> • In the absence of effective controls, the impact on operations is often significant. It can result in many of the following outcomes: <ul style="list-style-type: none"> – Additional training – New policies and SOPs – New work flow – Re-organization of personnel – Additional approvals and review periods from superiors – Heightened credentialing 	<p style="text-align: center;">Other Financial Repercussions</p> <ul style="list-style-type: none"> • Fines and penalties • Cost to enhance operations • Litigation and legal defense costs – considerable liability risk • Funding loss • Loss of brand equity, cost of damage to reputation and/or loss of community's trust....all are difficult to measure in real financial terms.

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Investigator Responsibilities

Introduction

- A Compliance Officer has many resources at its disposal to help mitigate risks associated with research administration.
 - Policies and SOPs
 - Training
 - Audits / investigations
 - Tone at the top
 - Threat of regulatory intervention
 - Law
 - Culture
- Given resources to “follow the rules” most will do the right thing.
- All research stakeholders are accountable for assisting the organization with fulfilling its compliance imperatives.

Any strong research compliance program is focused on Investigators. Ensure that they understand the responsibilities, are engaged in compliant behavior, and prioritize ethical research practices while maintaining institutional integrity.

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Collective Awareness Helps Foster Compliance

Investigator Responsibilities

- Among the most compelling allies that Compliance Officers have are Investigators... including Principal, Co-, and Sub-investigators.
- It is ESSENTIAL that all investigators understand their responsibilities.
- The responsibilities are formalized in the regulations and guidance provided by the following:
 - FDA: *FDA 21 CFR 312.60, 312.62, 312.64, 312.66, 312.68, 312.69.*
 - ICH/GCP E6 Section 4: *There is some overlap with the FDA regs.*
 - OHRP: *Regulations describe the duties of IRBs. IRBs, in turn, then create mandates for investigators. Most of these are covered in the FDA and ICH/GCP guidelines.*
 - NIH: *Policies describe the duties of the grantees, which in most cases are institutions. The institutions then create mandates for the investigators within their own policies.*



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Building and Sustaining a Research Compliance Program

Challenges

Expertise: Administering an effective research compliance program requires specialized understanding of key issues.

- Many professional organizations (e.g., SoCRA, ACRP, HCCA, SRA, NCURA and PRIM&R) offer comprehensive training programs tailored to the needs of different research stakeholders.
 - Investigators
 - Research staff
 - Compliance officers

Territorialism: Research programs present special challenges, as described, sometimes exacerbated by decentralized or siloed management and oversight functions.

Absence of Standards: Many research programs fail to build suitable training and education programs, document standards, or establish consistent workflow.

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Building and Sustaining a Research Compliance Program

Pragmatic Approach

- Engage investigators and research staff proactively
- Catalog mechanisms to identify potential deviations from legal/regulatory standards
 - Adverse event/deviation reports
 - Sponsor/CRO monitoring visits
 - Regulatory inspections – OHRP, FDA, etc.
 - Regulatory/guidance notices – determination letters, warning letters, etc.
 - Compliance reviews
 - Internal audits
- Require reporting to the HRPP leadership and the Compliance Officer of observed deviations
 - Research agreements
 - Institutional SOPs
 - Ensure that human subjects are fully informed of the risks and benefits of the research study in which they are participating.

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Building and Sustaining a Research Compliance Program

Understand the Legal Structure of the Research Enterprise

- Who is taking the money?
- Who is signing the Clinical Trials Agreement?
- Where are the protocol services occurring?
- What IRB is approving the study?
- Has there been an administrative 'OK' for the study?

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Building and Sustaining a Research Compliance Program

Key Elements

1. Leadership

- Research Compliance Officer or Deputy Compliance Officer with specific training, credentials, or a background in research compliance related issues.
- Research Compliance Committee. Ensure that a collaborative and diverse group of clinicians, support personnel, administrators, and compliance professionals are meeting to vet and discuss the unique compliance issues impacting the research program.
- Access to the Chief Compliance Officer and the institution's compliance committee.
- Independence and the ability to audit and monitor core research business practices.

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Building and Sustaining a Research Compliance Program

Key Elements

2. Auditing and Monitoring

- Perform annual risk assessment. Identify, rank, and prioritize auditing or monitoring plans to track and/or mitigate key risk areas.
- Establish sampling methodologies, error rates, and a documented set of responses and actions that the Research Compliance Program will take in the event that acceptable ranges of errors or non-compliance are exceeded.
- Document audit plans, monitoring activities and other focused initiatives in a Research Compliance Work Plan.

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Building and Sustaining a Research Compliance Program

Key Elements

3. Education

- Training can help demystify the regulatory environment and provide valuable knowledge to simplify the mounting challenges that researcher face.
- Because training is sometimes low priority and often seen as a time consuming, uninspiring, punitive, “check the box” type of activity by investigators, the need to develop a program that is fresh, useful and relevant to day-to-day issues is imperative.
- Consider linking CEUs or “research credentials” to the fulfillment of research training.
- Establish required training that goes beyond CITI. Customize training offering depending upon various categories of research stakeholders.
- Offer training a variety of mediums (i.e., webinar, brown bag, grand rounds, etc.).

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Building and Sustaining a Research Compliance Program

Key Elements

4. Policies and Standards

- Establishment of a Research Code of Conduct and/or a research supplement to the institution's code of conduct.
- Policy manual aligned with principles of human research protections, good clinical practices, NIH grants policy statement, CMS billing rules, FDA regulatory expectations, and the Office of Research Integrity.

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Thank You



Appendix



Investigator Responsibilities

FDA

- Follow the protocol and conduct the research in compliance with agreements and applicable regulations
 - Investigators must ensure that the investigation is conducted according to:
 - Signed investigator statement
 - Investigational plan
 - Applicable regulations
 - Investigators are protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation.
- Obtain the informed consent of each human subject to whom the investigational articles is administered
- Maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects.



Investigator Responsibilities

FDA

- Prepare and maintain adequate and accurate case histories
 - Investigators must record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.
- Retain records for a period of 2 years following the date a marketing application is approved or, if no application is filed, until 2 years after the investigation is discontinued and FDA is notified.
- Progress Reports
 - Furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained.
- Safety Reports
 - Promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug.



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Investigator Responsibilities

FDA

- Final Reports
 - An investigator shall provide the sponsor with an adequate report shortly after completion of the investigator's participation in the investigation.
- Financial Disclosures
 - The clinical investigator shall provide the sponsor with sufficient accurate financial information to allow an applicant to submit complete and accurate certification or disclosure statements as required under part 54 of this chapter.
- Assurance of IRB Review
- Permit FDA inspection of records and reports
- Take adequate precautions for the handling of controlled substances



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Investigator Responsibilities

ICH / GCPs

- Familiarity with the investigational product and research protocol and investigator's brochure
- Compliance with GCP and regulatory requirements
- Permit auditing and monitoring by the institution, the sponsor and regulatory agencies
- Maintain a list of qualified persons to whom duties have been delegated
- Demonstrated ability to recruit subjects within the given time period
- Sufficient time to properly conduct the trial
- Ensure that there are the proper number of staff persons and that they are trained on the protocol.
- Inform the participants' primary physician about enrollment on the study.
- Inform subjects of premature termination or suspension of the research