Objectives

At the conclusion of this session, the participant will be able to

- Describe the regulatory basis for establishing an audit and monitoring program
- Outline a business case for a viable audit and monitoring program
- Describe the necessary elements, specific to study sponsors, for an effective audit and monitoring program, including:
  - Audit content considerations for sponsor organizations
  - Scope development
  - Sampling techniques
  - Reporting
Current Regulatory Environment

What Are The Major Regulatory Factors Impacting Clinical Research Studies?
Life Sciences and Health Care Organizations operate in an increasingly complex environment including…

- International regulations
- Federal and State regulations
- Enforcement body guidance and rulings
- Regulatory enforcement findings

In addition to the regulatory requirements, organizations must also understand the following…

- Contractual requirements
- Internal company policies and standards
- Industry Standards (FDA, the Centers for Medicare and Medicaid Services)
What are sponsors responsible for from a regulatory perspective?

- Obtaining agency approval where necessary
  - IND application (investigational drugs)
  - IDE application (investigational devices)
- Manufacturing and labeling investigational products appropriately
- Initiating, withholding, or discontinuing clinical trials as required
- Refraining from commercialization of investigational products
- Selecting qualified investigators to conduct studies
- Disseminating appropriate information to investigators
- Selecting qualified persons to monitor the conduct of studies
- Adequately monitoring clinical investigations
- Evaluating and reporting adverse experiences
- Maintaining adequate study records
- Submitting progress reports and the final study results
Quality, compliance and business risks managed in silos: Many regulatory components, some repetitive, some conflicting
“Although many monitoring techniques are available, one effective tool to promote and ensure compliance is the performance of . . . compliance audits by internal or external auditors who have experience on federal and state health care statutes, regulations and federal health care programs.”

HHS Office of Inspector General
### Foundational Concepts

Why develop an organization-wide compliance strategy: Proactive vs. Reactive?

<table>
<thead>
<tr>
<th>Being Proactive</th>
<th>Being Reactive</th>
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<tbody>
<tr>
<td>✓ Develop a process to efficiently and effectively manage risk for the organization</td>
<td>✓ Inconsistent application across the organization</td>
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<tr>
<td>✓ Capability to expand on business opportunities (e.g., product development or management)</td>
<td>✓ Potential individual civil / criminal liabilities</td>
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<td>✓ Achieving a market leadership position</td>
<td>✓ Reputation risk</td>
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<td>✓ Restriction of business operations imposed by regulators</td>
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The Business Case for a Strong Internal Control Program

The Upside
- Make better business decisions with higher quality, more timely information
- Reduce potential for fraud
- Gain (or regain) investor trust
- Prevent loss of resources
- Comply with laws and regulations

The Downside
- SEC sanctions
- Unfavorable publicity
- Negative impact on shareholder value
- Misappropriation of assets
- Lawsuits or other legal actions
Goals of a Comprehensive Audit and Monitoring Program

Early Warning Systems
- Systematically identify, assess and prioritize risks
- Avoid unrewarded risks and protect assets in place
- Promote organizational learning
- Reduce chance of repeat problems

Integrated Infrastructure
- Ensure bad news travels fast internally first – early warning systems
- Prevent and rapidly respond to potential catastrophic failures
- Improve ability to anticipate and prepare for change
- Establish a risk-based culture
- Provide assurance that key risks and exposures are understood and mitigated

Comprehensive Policies & Procedures
- Seek growth but ensure strategic and tactical risks are mitigated
- Maximize chances of success of achieving business plan goals
- Accelerate ability to respond to change and opportunities
- Install an appropriate control infrastructure

No Big Surprises

No Big Missed Opportunities

No Big Mistakes
Applying Compliance into Operations

**Mission & Objectives**
- Identify key high risk areas relating to regulatory requirements

**Risk Assessment**
- Prioritize Risks
- Evaluate Implementation Plans
- Compliance with Applicable Rules and Regulations

**Audit Plan**
- Risk/Control
- Management Focus

**Audit Testing**
- Best Practices/Benchmarks
- Assessment Checklists
- Self Evaluation

**Reports & Feedback**
- Recommendations
- Performance Assessment
- Special Audits
Methodologies: Create a Compliance “Cross Walk”

- Monitoring Plan Should Be Designed With The Compliance Program Dilemma In Mind.
- Monitoring Creates The Crosswalk Between The Business Strategies And The Risk Areas

Vaccines Will Be Available to the Public

Business Strategy
Will be impacted by many risk areas

Risk Area
Apply to more than one business strategy
Auditing and Monitoring Cycle

Define Review Scope & Assumptions

Review Process for Each Risk Area

Develop Review Criteria

Define Review Sample

Test Inter-rater Reliability with multiple reviewers

Conduct Review

Validate findings

Define Methodology

Education, remedial action

Finalize Report & Corrective Action Plan

Obtain Management Response

Document Observations & Findings

Reaudit
Potential Audit Topics

- Regulatory compliance
  - IRB approval of protocol, informed consent
  - 1572’s
  - Conflict of Interest
  - Required training completion
  - Communications between sponsor, IRB, investigator
- Recruitment activities
- Study Participant records
  - Eligibility
  - Consent
  - Treatment
  - Adverse Events
  - Response
  - HIPAA related privacy
    - Permissible uses and disclosures
    - Elements of a valid authorization
Potential Audit Topics

- Study protocol compliance
- Study drug or device
  - Inventory controls
  - Storing
  - Compounding
  - Dispensing
- Adverse events or complications
- Response
- Data management
  - Case report forms
  - Data integrity, quality control
  - HIPAA related Security
- Billing Issues
- Accounting
Focus Area: Stark Law

Stark Law—General Rule
- If physician-investigator makes referrals to facility for designated health services (“DHS”), financial relationship must comply with Stark exception
- Failure to comply means DHS referrals are prohibited; facility can’t bill Medicare/Medicaid for services provided pursuant to prohibited referral
- Civil monetary penalties, possible False Claims Act liability

Primary exceptions for arrangements involving payments to investigators
- Bona fide employment relationships
- Personal service arrangements
- Fair market value compensation

Other potential financial relationships
- Rental of office space or equipment to investigator
- Provision of staff or support services to investigator
Compliance Tips

- Identify all financial relationships between sponsor and investigator
- Review terms of each financial relationship (as reflected in a written agreement, where required) for compliance with a Stark exception
- Review payments to investigators to confirm they are consistent with the terms of the Stark-compliant agreements
- Promptly fix any arrangements that have fallen out of compliance with Stark (or that didn’t comply in the first place)
  - New Stark II, Phase II regulations have exception for temporary noncompliance
    - Must have been in compliance for 180 days
    - Noncompliance not within entity’s control
    - Relationship doesn’t violate anti-kickback statute; bill/claim complies with all other laws/regulations
    - Only applies for first 90 days after noncompliance starts; can only use once every three years for a particular investigator
  - If exception isn’t available, don’t submit claims during period of noncompliance
Focus Area: Anti-Kickback Statute

- Prohibits, among other things, soliciting, receiving, offering or paying any remuneration in return for referring a patient or to induce the referral of a patient to any person for any item or service for which payment may be made under a federal health care program

- Safe harbors are available
  - Bona fide employment relationships
  - Personal services and management contracts
  - Space and equipment rentals

- Compliance tips
  - Review all financial relationships with investigators who make or can influence referrals
    - Fit within safe harbor where possible
    - In all cases, ensure compensation paid by either party is consistent with fair market value
    - Ensure that there is no intent to induce referrals in violation of the statute
Focus Area: Stark and Anti-Kickback Auditing

- Key Elements for Relationships
  - Written agreements
  - Signed by the parties
  - Fair market value compensation, set in advance
  - No services for payment until agreement is signed
  - Minimum term of one year
  - Compensation does not vary by value/volume of referral
Focus Areas: Stark and Anti-Kickback Contract Review

- Possible Approach:
  - Review accounts payable ledger for all physician payments
  - Check for contract to support each payment
  - Evaluate payments for consistency with contract terms and required elements
  - Review time logs where appropriate
  - Types of contracts for possible consideration:
    - Space Rentals
    - Equipment Rentals
    - Medical Director Agreements
    - Call Coverage Agreements
Uses and disclosures of protected health information (PHI) for research purposes
- Written authorization
- Reviews preparatory to research
- Disclosures to the patient
- IRB or Privacy Board waiver of authorization
- Limited data set (with data use agreement)
- Public health activities (disclosures to monitors)

Business associates?
- OCR position: research is not a HIPAA covered function or one of the services listed in HIPAA’s definition of a “business associate”
- Business associate contract (BAC) not needed between covered entity and researcher
- Even if use BAC, can’t disclose PHI to researcher unless one of the above exceptions applies
Focus Area: Elements of HIPAA Authorization

- Description of information to be used or disclosed
- Identification of person(s) authorized to make the use or disclosure
- Identification of person(s) to whom disclosure may be made
- Description of each purpose of the use or disclosure (can’t authorize use or disclosure for future, unspecified research)
- Expiration date or expiration event (not required for research)
- Signature and date
- Statements adequate to put the individual on notice as to:
  - Right to revoke in writing (including any exceptions)
  - Ability or inability to condition treatment, payment, enrollment or eligibility for benefits on the authorization
  - Potential for information to be redisclosed by recipient and no longer protected by HIPAA
HIPAA: Compliance Tips

- Review subject screening and recruitment practices for HIPAA compliance
- Ensure all investigators, recruiters, and other personnel are aware of HIPAA requirements
- Obtain HIPAA-compliant authorizations from subjects as early as possible in the recruitment process
- Need to track disclosures (but not uses) of PHI for research to be able to provide an accounting of disclosures
  - Accounting requirement does not apply to disclosures to patient/subject, disclosures pursuant to written authorization, or disclosures as part of a limited data set
- Don’t rely on business associate contract to make disclosures of PHI for research
Steps in the A&M Process

I. Develop Review Criteria
II. Define the Sample
III. Select Methodology of Review
IV. Determine Inter-rater Reliability
V. Validate Findings
VI. Document Observations and Findings
VII. Corrective Action Plan
VIII. Remediation
Reports and Feedback

- Recommend corrective measures, including the development of revised policies and procedures to meet regulatory requirements
- Significant findings and action taken should be documented and communicated to senior and governance leadership
- Performance assessment of trends identified as control weaknesses and compliance violations
- Re-audit as necessary based upon initial findings and associated risk
- Conduct Special Audits, as needed, i.e. follow up after resolution processes put into place
# Corrective Action Plan

<table>
<thead>
<tr>
<th>Area of Focus</th>
<th>Finding</th>
<th>Recommendation</th>
<th>Management Action Plan Acct/Timeframes</th>
</tr>
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<tbody>
<tr>
<td>1. Contract load</td>
<td>1. 20% data errors in contract load</td>
<td>Periodically review data entry</td>
<td>Develop a periodic review system</td>
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<tr>
<td></td>
<td>2. Etc.</td>
<td>Etc.</td>
<td>John Smith, VP</td>
</tr>
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<td>Etc.</td>
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Considerations

- Who needs to know about findings
- What is the “frame of reference”
- When is the best time for reporting results
- How should you communicate, ie: summary, verbally, factual information related to error rate, etc.
An effective Auditing and Monitoring approach provides a method to:

- Assist in identifying risk to the business that may have been otherwise undetected internally
- Assist by identifying if the controls developed to remediate a risk are working and have actually helped to mitigate the risk
- Assist with preventing a real and/or potential risk from escalating by early detection through auditing which may help avoid additional harm to the company’s business
- Provides a “good faith” organization the ability to approach their real and/or potential risk weaknesses with a reasonable, scaleable method

Auditing and Monitoring is a critical element for an effective compliance program which helps to drive compliance and behavior.
Monitoring never ends… each review leads to the next, and the monitoring plan and unplanned issues drive additional review activities. It is a continuous process…
Questions/Answers