

Regulatory Visits, Audits and Investigations

The Role of the Compliance Officer

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Welcome!

The content of this presentation does not necessarily represent or reflect the views of the institutions with whom the presenters are affiliated.

Today's Objectives

- Setting the stage
 - Describe the environment
 - What is our context?
- Compliance Officer relationships to:
 - Organizational leadership and the Board
 - Office of Counsel
 - Internal Audit
- The "lifecycle" of regulatory visits, audits and investigations
- Review and clarify concepts
 - Auditing, monitoring
 - Investigations, reviews
 - Quality assurance/quality improvement
 - Critical Terms: Civil Investigative Demands, Subpoenas, Search Warrants
 - Behavior while under scrutiny
- Getting down to the basics – Templates, checklists, forms, yeah!

Setting the Stage

- Evolution of Expectations
 - From "Do the Right Thing" to documentation and verification that the right thing has been done (including remediation when facts indicate otherwise) "pushing" emergence of "culture of integrity"
- Why?
 - Failure of institutions and leadership to practice and enforce ethical and appropriate organizational behavior
- Resulting In
 - Abuse of Human and Animal Research Subjects, Loss of Public Trust, Tarnished Reputations, Fines, Sanctions, Decreased Funding (Grants)

And ...

What are the Laws and Regulations

- False Claims Act, 1863
- Human Subjects Protection (Common Rule), Nuremburg Code, Decl. of Helsinki
- Federal Sentencing Guidelines and Amendments
- Sarbanes-Oxley (Internal controls and Non-retaliation against "whistleblowers")
- Privacy Legislation (HIPAA/HITECH, Gramm-Leach-Bliley, State Identity Theft Protection Statutes, Red Flags)
- Patriot Act, Foreign Corrupt Practices, Export Control, etc.
- Evolving complex, often inscrutable, compendium of "Guidelines" from every administrative unit with oversight responsibility/authority
- Others?
- Your institution's own policies?

Federal Sentencing Guidelines have become the catechism for Compliance

- ❑ The organization's leadership and governing authority must be knowledgeable about the content and operation of its compliance program
- ❑ The organization's governing authority must exercise reasonable oversight regarding the implementation and effectiveness of the program
- ❑ Specific high-level personnel must be assigned direct responsibility for ensuring implementation and effectiveness of the compliance program
- ❑ Such personnel must be given sufficient resources and report directly to the governing authority or appropriate subgroup of the governing authority

Federal Sentencing Guidelines have become the catechism for Compliance

- ❑ The organization must institute effective training programs for the governing authority, leadership, employees, and, as appropriate, agents
- ❑ The organization must audit and monitor its program for effectiveness and conduct ongoing risk assessments to refine its program and reduce the risk of violations
- ❑ The organization must have an anonymous reporting system for employees
- ❑ The organization must establish appropriate incentives and disciplinary measures to ensure reporting, compliance, and correction of violations

Compliance Officer Relationships

- ❑ Organizational leadership and the Board
- ❑ Office of Counsel
- ❑ Internal Audit

Building an internal compliance network

- ❑ Compliance Leadership Group
- ❑ Compliance Liaisons
 - A Compliance Liaison is a representative to person(s) charged with compliance *operational* responsibilities for a particular area (the true warriors)
 - Liaisons serve as both ambassadors and antennae -

Lifecycle of Regulatory Visits, Audits and Investigations

□ Why might we be visited?

- Not for probable cause (sampling) review
 - Effort reporting, Conflict of Interest, HIPAA Security
- Provision of funding award, contract, sponsored research agreement
- Agency quality assurance
- False claim
- Billing
- Accreditation
- Failure to provide timely reports, or troubling report
- Receipt of "expression of concern"
- Self report (may arouse interest in other areas)
- **Also note:** concern may relate to event or set of circumstances at another institution

How Might We Be Contacted

- With notice
 - Formal letter
 - Telephone call/e-mail
- Without notice
 - "Surprise" visit (perhaps call from a staff assistant or registrar)
- **Note:** it is a good idea to have a policy in place that requires Office of Counsel and Compliance Officer be advised immediately however notice is received

Preparing for the Visit

- ❑ Identify a "project manager" – Likely Compliance Officer Role
- ❑ Assemble a project team (should include P.I. or other high ranking responsible party)
- ❑ Draft preparedness timeline, task/responsibility list
- ❑ Attempt to get agenda
- ❑ Organize records (consider time needed to retrieve from storage) – see Regulatory Binder checklist, at end
- ❑ Review records access needs and requirements (consider time for systems to admit new users, control and monitoring of access, etc.)
- ❑ Identify applicable governing regulations, institutional policies, websites, **training**
- ❑ Attempt to determine who might be interviewed and provide guidance on proper behavior, communication
- ❑ Identify space for visitors to work, administrative assistance – but, also consider managing their access to your facilities ("temporary" i.d. badges, etc.), escorts
- ❑ Assign tasks for receiving visitors: appropriate level of institutional official should welcome, identification/authentication should be secured, if "controlled" area, evidence of proper vaccination should be produced
- ❑ Anticipate areas to be visited (labs) and train **everyone** likely to be engaged
- ❑ If visitors are non-US, consider that their documentation might not comply with your institution's policy requirements.
- ❑ Determine who should attend opening and closing conferences

They're here

- ❑ Opening conference
 - Check/verify credentials
 - Review agenda, expectations, including anticipated length of visit, logistics
 - Make notes of discussions
- ❑ During the visit
 - Make a copy of documents visitors request, note circumstances of request
- ❑ Closing conference
 - Visitor team leader will likely review findings, advise when final, written report to be expected, and response opportunity

*** Pay attention to deadlines ***

*Visits for which you have **no** notice*

- Nothing instills greater anxiety for the compliance officer/counsel
- Visitor may present with:
 - Search warrant
 - Deposition (unlikely, as these generally forwarded to Counsel)
 - Civil Investigative Demand (not as common)
- If it is a search warrant, make sure it is authentic (ask Counsel to determine)
 - Ensure "scope" properly managed, and, if not, object and note, but do not interfere
 - Yep, they can even take the sticky-notes and trash ...

When, they're gone ...

- Summarize the visit, observations
- ... the wait (for the report) begins
- Always consider: in your preparation, have you discovered any situations that need resolution/remediation?
- Outside expertise may be very helpful!
- Your work may have only just begun: technical "findings" may be relatively insignificant, but identify systemic weaknesses that are expensive to fix

Your institutional policy re Regulatory Visits, Audits and Investigations

- ❑ Communicate with leadership re the need for formal approach
- ❑ Ask departments/divisions for representatives (compliance liaisons?)
- ❑ Train re need, appropriate behavior – again, they are your “ambassadors” in their respective areas
- ❑ Reduce to policy; publish; “remind” on yearly basis, train new administrators

Monitoring vs. Audit

Monitoring:

- ❑ Performed by personnel charged with trial compliance operational responsibility; regular, on-going

Audit:

- ❑ Ensures that those with trial compliance responsibility are doing what they have been charged to do (by all governing sources). Independently verified, not operational, may be internal or external to the institution

Regulatory Binder Template

- A regulatory binder contains all vital study documentation and is maintained by the principal investigator or his/her designee. The regulatory binder is required for all clinical trials, but its list of contents is useful for organizing records for any study. The regulatory binder should include the following items:
 - Protocol
 - Consent Form Document
 - IRB approval/correspondence
 - Sponsor correspondence (if applicable)
 - Signature list of research staff and their role responsibilities
 - Serious Adverse Event reports
 - Monitoring/Audit log reports
 - Final study reports
 - Investigator's brochure or package insert
 - Standard operating procedure manual
 - FDA Form 1572 (or Investigator's Agreement- if applicable)
 - Laboratory certification (if applicable)
 - Range of normal laboratory values (if applicable)
 - Drug/device accountability documentation (if applicable)
- This binder should be maintained on a regular basis and items filed in reverse chronological order.

Final Notice of Review

□
[Date]
RE: [Protocol Name and IRB Number]
Dear Dr []:

This letter is to confirm a Clinical Trials Quality Assurance Review of the above-referenced protocol in which you are involved as the Principal Investigator. The review has been scheduled with [coordinator's name or office staff that scheduled] for [date(s) and time(s)]. I plan to arrive at [time] and complete the review by [time and day].

This review is being conducted to assess that this protocol as approved by the University Health Systems Institutional Review, is being conducted in accordance to FDA regulations, Good Clinical Practice (ICH guidelines), and University Health System institutional guidelines.

Upon my arrival, I will be conducting an opening meeting with you and your study coordinator, [coordinator's name] and other parties that you deem appropriate to attend. This meeting will take approximately 30 minutes and will provide me with a general overview of the study as it has been conducted at your site. I will be available to answer questions that you may have about the review procedure. I will schedule a convenient time for a closing meeting near the end of the audit. All parties attending the opening meeting must be present at the closing meeting.

I will require the following items be made available to me during my visit:

- Consent forms for all subjects
- Essential Documents and/or Regulatory Binder (study protocol, FDA 1572, IRB documentation and correspondence, delegation of authority log, all other correspondence, etc.)
- All case report forms, medical records and additional source documentation for the following subjects: [subject codes here]
- All adverse event/MedWatch reports
- Records regarding the research article storage, distribution, and accountability
- Standard Operating Procedures (SOPs)
- Site activity areas (such as file storage, subject examination areas)
- To expedite the review process you may send the following items to the CTQA office prior to the scheduled review. Please coordinate this with the CTQA office.
- SOPs
- Organizational charts
- Delegation of Authority Log
- Curriculum Vitae and Certifications/Licenses

Your cooperation with this review visit is sincerely appreciated. I look forward to meeting you and working with your staff during this visit. If you have any questions, please feel free to call me at (000) 000-0000.

Sincerely yours,

cc:

Regulatory Document Tracking Log

Document	Version #/date	Date Signed by PI	Date to sponsor	Date to IRB	IRB approval date	Expiration Date	Comments
Investigator Brochure							
Protocol							
Amendment #							
Amendment #							
FDA 1572							
FDA 1572 Revised							
CV and Medical License							
Consent Document							
Consent Revision							
Advertisement							
Certificate of Confidentiality							
Periodic (Annual) Report							
Final report							

SIGNATURE AND DELEGATION OF RESPONSIBILITY LOG

Investigator: _____ Site: _____ Effective Date: _____

Protocol Number/Title: _____

Name (Please Print)	Title	General Responsi- bilities	C.V. Available	Dates of Responsibilities		Signature	Initials	Approved (PI Initials)
				To (dd/mm/yy)	From (dd/mm/yy)			
			<input type="checkbox"/> Yes <input type="checkbox"/> No					
			<input type="checkbox"/> Yes <input type="checkbox"/> No					
			<input type="checkbox"/> Yes <input type="checkbox"/> No					
			<input type="checkbox"/> Yes <input type="checkbox"/> No					
			<input type="checkbox"/> Yes <input type="checkbox"/> No					
			<input type="checkbox"/> Yes <input type="checkbox"/> No					
			<input type="checkbox"/> Yes <input type="checkbox"/> No					
			<input type="checkbox"/> Yes <input type="checkbox"/> No					
			<input type="checkbox"/> Yes <input type="checkbox"/> No					
			<input type="checkbox"/> Yes <input type="checkbox"/> No					

This log should include the investigator and sub-investigator(s), study coordinator(s) and all other clinic staff who routinely see study subjects and who have specific data collection/interpretation/management responsibilities. This log should also include any contracted specialists performing protocol required examinations. New or replacement staff should be added as appropriate.

* Please see Legend (page 2 of 2)

PLEASE MAINTAIN THIS LIST WITH YOUR REGULATORY FILES

SIGNATURE AND DELEGATION OF RESPONSIBILITY LOG

Legend

Use legend to complete the "General Responsibilities" column. Please enter the letter(s) (i.e. ace) in column that corresponds to the responsibilities of the individual. For responsibilities that are not already indicated in the legend, please add them in the empty spaces provided below.

- a Obtains consent*
- b Completion of CRFs
- c Correction of CRFs
- d Review of CRFs (must be investigator or sub-investigator)
- e Communication with IRB*
- f Physical exam*
- g Calculation of dosage*
- h Titration and prescription
- i Dispensing of investigational item
- j Investigational Item compliance assessments
- k Investigational Item accountability
- l Inter-rater reliability assessments
- m Collection of Adverse Events*
- n _____
- o _____
- p _____
- q _____
- r _____
- s _____
- t _____

* Identifies functions which are significant trial-related duties and for which curriculum vitae of personnel MUST be obtained and on file.

PROTOCOL VIOLATION TRACKING LOG

Principal Investigator: _____

IRB Protocol #: _____

Study Title: _____

Sponsor: _____

Subject	Date of Violation	Major/Minor	Description	Date of IRB submission	Date of IRB Notification (i.e. response)	Date Sponsor Notified	Date of Sponsor Approval
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							
11							
12							
13							
14							
15							

** Report all violations/deviations/exceptions in accordance CTQA and IRB Policy

Clinical Trials Quality Assurance
Quality Assurance/Peer Review Materials: Confidential and Privileged Under State Law

Protocol Review Report

Review Number: _____ Assigned Reviewer: _____
 Review Start Date: _____ Review End Date: _____

Protocol Number: _____
 Protocol Title: _____
 Research Article (if any): _____

Principal Investigator: _____
 Department/Division: _____
 Primary Study Coordinator: _____
 Additional Key Personnel: _____

Previous CTQA Reviews?: _____
 Yes (If Yes, continue) No
 Date(s): _____

Have there been FDA audits (if applicable) within the past 5 years?
 Yes (If Yes, continue) No

Date(s): (start with most recent) _____ 483's _____ Warning Letter _____
 Yes No Yes No
 Yes No Yes No
 Yes No Yes No
 Yes No Yes No

Final Classification:
 No Actions Indicated
 Voluntary Actions Indicated
 Official Actions Indicated

Corrective Action Due Date: _____

Number of Subjects Reviewed: _____
 Number of Informed Consents Reviewed: _____
 Consent Process Reviewed: Yes No

Clinical Trials Quality Assurance
Quality Assurance/Peer Review Materials: Confidential and Privileged Under State Law

Protocol Review Report

Review Number: _____ Assigned Reviewer: _____
 Review Start Date: _____ Review End Date: _____

REVIEW SUMMARY

Scope

The purpose of this review was to assess the adherence to the Institutional Review Board approved study protocol, Good Clinical Practices (GCPs) guidelines, and State and Federal Regulations; to determine that the rights and welfare of human research subjects are being or have been adequately protected by the Investigator and his/her research staff; and to assess the integrity of the study data.

During this review, the study specific regulatory files, departmental Standard Operating Procedures (SOPs), ___ subject files and appropriate source documentation were reviewed.

Introduction

This is a principal investigator initiated Phase I protocol to examine _____. The protocol has received no prior FDA or CTQA review. At the time of this review, the site had screened ___ subjects and had enrolled ___ subjects to the study drug. ___ subjects remain active on the study, ___ subjects have completed the study, ___ subjects discontinued from the study due to adverse events and ___ subjects withdrew consent. There have been ___ reported Serious Adverse Event (SAEs) related to this protocol. [Provide additional Information and Details]

This study is being conducted by [PI name], Dr. _____ has been in practice at University Medical Center since _____. He/she is board certified in [specialty]. Dr. _____ devotes approximately _____ time to private practice and _____ to research. Dr. _____ is involved with _____ clinical trials as the PI and has been involved in clinical research for _____ years.

Dr. _____ has the responsibility of Principal Investigator for this trial. Dr. _____ is supported in this study by sub-investigators, a primary study coordinator and _____ additional coordinators. Dr. _____ is responsible for [list duties in narrative form], _____ is the primary study coordinator, his/her responsibilities include [list duties]. The additional coordinators are responsible for [duties].

The first study subject to screen for this clinical trial was screened on [date]. A total of ___ subjects have been screened and ___ subjects have randomized into the trial. To date the subjects have been recruited from [recruitment methods, if advertisements state if IRB approved].

This was a routine Clinical Trials Quality Assurance review performed per the Clinical Trials Quality Assurance Review Standard Operating Procedures. The following is a summary of this methodology:

- Review of internal study files
- Opening meeting (initial introductions and interviews with PI and key staff)
- Facilities assessment
- Review of study/regulatory file and storage
- Source document verification
- Review of Consent Documents
- Review of research agent accountability records and storage

Executive Summary:
Overall Review Assessment

Clinical Trials Quality Assurance
 Quality Assurance/Peer Review Materials: Confidential and Privileged Under State Law
 Protocol Review Report
 Review Number: _____ Assigned Reviewer: _____
 Review Start Date: _____ Review End Date: _____

Dr. _____ and the study staff interviewed demonstrated knowledge of the protocol and study requirements, and the delegation of duties appeared to be adequate. Dr. _____ was aware of his/her responsibilities as a Principal Investigator under the regulations and guidelines for the conduct of research trials and demonstrated that he/she was an integral part of the study and safety review process.

Study documents for all subjects reviewed were found to be present. Study specific regulatory files were substantially complete, and the facility appeared adequate for the study (i.e. physical environment, waiting area, etc.).

Overview of Review Observations: (Please see the observations table below.)

The review concluded that voluntary corrective actions listed below are appropriate. There were ___ level 1 observations and ___ level 2 observations noted.

Observation Number	Observation/Corrective Action	Category (1-2; R or C)	Level of Significance (1,2,3)	Frequency (number of instances)
1	Corrective Action: [Type response here] Date to Complete:			
2	Corrective Action: [Type response here] Date to Complete:			
3	Corrective Action: [Type response here] Date to Complete:			

Conclusions

How much does this all cost?.....

And, how much can this save?.....

Conclusion ...

Are we there yet?

Questions?

Thank you!

(Please remember to turn in your evaluations)