STATEGIES TO PREVENT FDA INSPECTION FINDINGS

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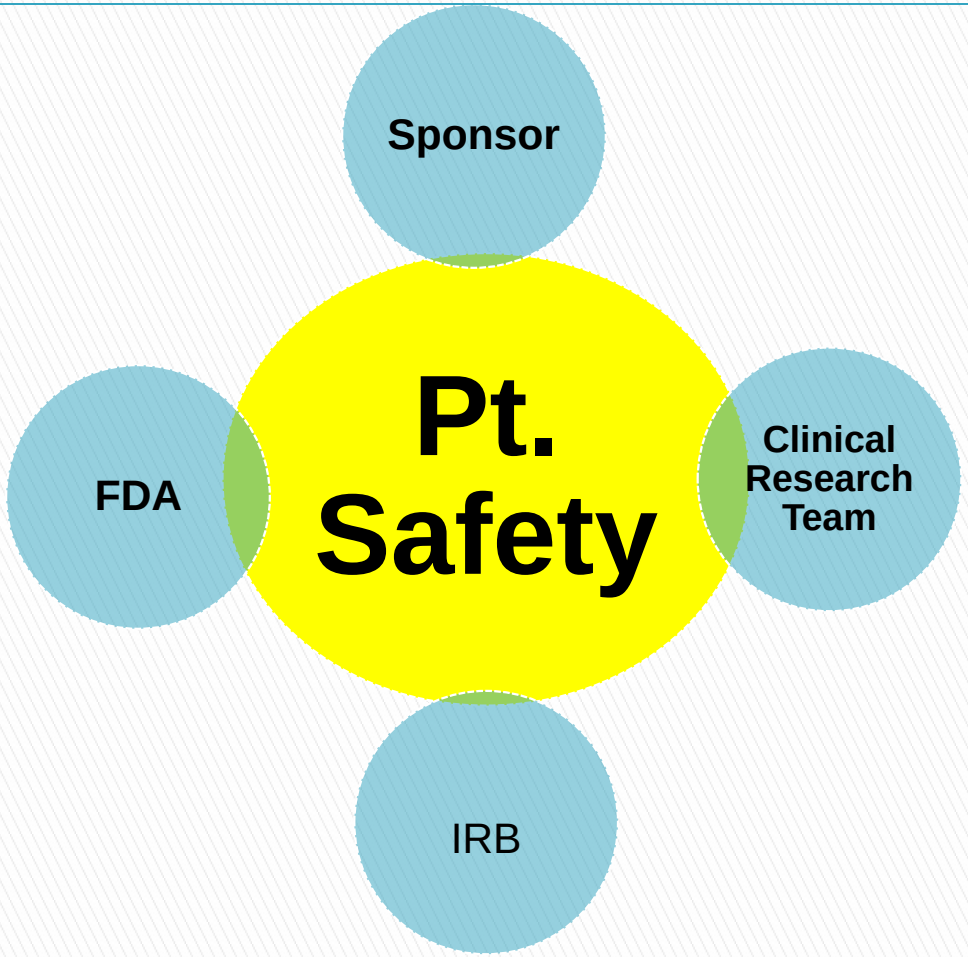
Objectives

- **Understand** the Responsibilities of FDA, Sponsor, and Investigator
- **Prepare** for a FDA Site Inspection
- **Determine** Best Practice for Hosting a Site Inspections
- **Know** what Sanction of Inspection finding

Question

What do the FDA, Sponsor, Research Team, and the IRB all have in common ?



Answer!

- **Same Goals:**

To identify and promote practices that will increase the quality and efficiency of clinical trials

- **Same Vision:**

A high quality clinical trial system, that is patient-centric, efficient, and produces timely access to evidence-based prevention and treatment options

- **Same Results:**

To conduct successful Clinical Trials!

To improve the efficiency of bringing new products to market without diminishing human subject protection

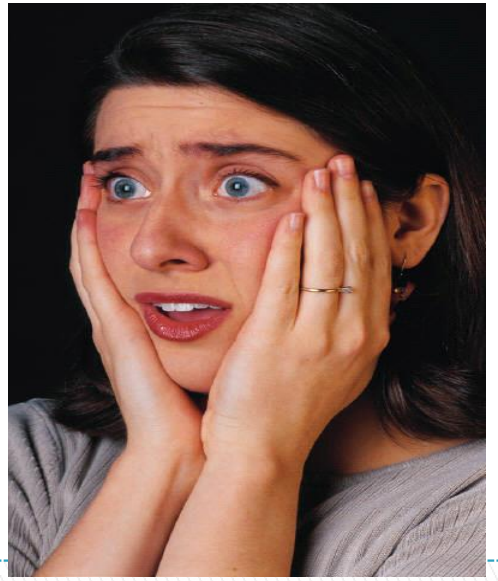
- **Promote:**

Confidence in the clinical trials process

Scenario: of FDA Inspection

The receptionist/Data Coordinator has just walked into your office and said the following to you:

There is a man out at the desk, say's he is from the FDA!



- She asks **you** what she to do?

Group Instructions:

Given the Scenario design your strategy for how to handle the situation

You retrieve the SOP for your site on

How to Conduct an FDA Inspections, along with a checklist for inspection.

Your management team is offsite for a meeting for the day and will return in the morning. The Principle investigator is unavailable for the next hour.

Divide into Discussion Groups A,B,C

FDA Compliance Program Guidance Manual-Program 7348.811

- Bioresearch Monitoring Clinical Investigator and Sponsor-Investigator
- Guidance for the FDA
- Field Reporting Requirements: How to Establish Inspection Reports.

Group A: Data Coordinator or Research Nurse Preparing for Inspection

- What document outlines the steps for preparing for the inspection?
- What documents are you going to have ready for the inspection?
- Can the inspection checklist be used in preparation for an inspection?
- Who should you notify of the inspection and when should they be notified: (announced and unannounced)
- Who Should participate in the Inspection?

Group B: Hosting the Inspection

- What document outlines how to host the inspection?
- What documents will you request upon the arrival of the inspector ? What Identification?
- How can the inspection checklist be used?
- What are the roles of the site personnel that take place in the inspection?
- What are the Do's and Don't of the inspection
  - *location of inspection
  - *how should conversation be handled?
  - *what should happen at the end of every day

Group C: FDA Inspectors

- What document Identifies what the inspectors will be looking for?
- What are three specific reasons an inspection can be done? (on Checklist).
- What 5 categories are covered in the inspection check list?
- What Guidance for FDA Staff describes what the field reporting Requirements are?
- Describe what document is issued with inspection observations?

Responsibilities

- Investigator- The Individual that actually **conducts** the a clinical trial
- Sponsor -Individual or company who **takes responsibility** for and **initiates** a clinical trial.
- Sponsor /Investigator-(individual) **Initiates and is responsible for conduct of the trial.** The sponsor can actually be the Principle investigator as well if he is a sponsor and investigator.

Responsibilities: Principle Investigator

Signing a 1572 commits an investigator to :

- **Conduct** the study according to the protocol
- **To personally supervise** or conduct the investigation of the clinical trial.
- **To inform** the subjects of the investigational status of the test articles
- **To report** adverse events to the sponsor
- **The read and understand** the Investigator Brochure
- **To inform** all support personnel of the investigator requirements

Investigator: Signing a 1572 (cont.)

- maintain adequate records and make them **available for inspection**
- Assume responsibility for initial and continuing review by the IRB
- NOT make any changes in the research protocol with IRB approval
- To comply with the requirements regarding the obligations of clinical investigator
- *WARNING- a willfully false statement is a criminal offense*

Responsibilities of the Sponsor signs a 1571, agrees to:

- Not begin or continue the study if placed on hold
- IRB will be responsible for review and approval of the study.
- To conduct the study in accordance with all applicable regulatory requirements
- WARNING: A willfully false statement is a criminal offense.

Responsibilities of the Sponsor signs a 1571

21 CRF 812.20 subpart C

- FDA and IRB approval
- Selecting investigators and monitors
- Informing investigators and monitors
- Informing investigators
- Monitoring investigators

2012 Inspection Findings Most Common CI Deficiencies

- Failure to follow the investigational plan and/or regulations
- Protocol deviations
- Inadequate recordkeeping
- Inadequate accountability for the investigational product
- Inadequate communication with the IRB
- Inadequate subject protection (including informed consent issues)

2012 Inspection Findings
Most Common IRB Deficiencies

- **Inadequate initial and/or continuing review**
- **Inadequate SOPs**
- **Inadequate membership rosters**
- **Inadequate meeting minutes**
- **Quorum issues**
- **Inadequate communication with CI/institution**
- **Specific to devices – lack of incorrect SR/NSR determination**

2012 Inspection Findings
Most Common S/M/CRO Deficiencies

- Inadequate monitoring
- Failure to bring investigators into compliance
- Inadequate accountability for the investigational product
- Failure to obtain FDA and/or IRB approval prior to study initiation

2012 Inspection Findings Common Deficiencies

- **Record keeping**
- **Protocol deviations**
- **Dosage Issues**
- **Analytical Concerns (validation, stability)**

2012 Inspection Findings ~Deficiencies~

- Organizational and/or Personnel inadequacies
- Incomplete/inadequate/no study records
- Inadequate/no standard operating procedures (SOPs)
- Protocol deviations
- Incomplete/inaccurate study reports

Strategies to conduct a qualified device study

- Selecting qualified investigators
- Obtain feedback on protocol requirement
- Provide training up front
- Ensure adequate monitoring
- Adequate facilities
- Sufficient number of staff
- Feasibility of tests

Site Conduct

- **Common factors that may affect the ability to provide adequate supervision for trials.**
  - **Inexperienced study staff**
  - **Demanding working load**
  - **Complex clinical trials**
  - **Conducting multiple trials concurrently**
  - **Subject population that is seriously ill**
  - **Conducting a study at multiple sites under the oversight of a single PI**

2012 Inspection Findings
Most Common International Deficiencies

- **Similar to domestic inspectional findings**
- **Sponsor inspections (inadequate monitoring; failure to bring investigators into compliance)**
- **CI inspections (protocol deviations; Inadequate investigational product accountability; inadequate subject protections**

Take home – Panel Discussion

- Notes to File – excessive NTFs will cause a red flag that something is wrong. It may expose a 'process problem.'
- Keep straight what the sponsors want reported and what the IRB wants reported. It may not be the same.
- FDA does not want to 'double-regulate' products..Biologic/Device if it already has an IND, it does not need an IDE. FDA departments will work together.

Take Home – Safety

- Stand up to issues that affect patient safety!
- Have Quality Assurance Practices that maintain Subject Safety
- Use pre-printed order sets
- Use units of measure when recording data
- Coordinate research staff with clinical staff providing care

USF -This is the link to the HRPP policies: http://www.research.usf.edu/dric/hrpp/policy-procedure.asp

FDA Sources

- www.fda.gov
- www.fda.gov/Drugs
- www.fda.gov/biologicsBloodVaccine
- www.fda.gov/bsufa
- www.fda.gov/Drug/developmentApprovalProcess/howDrugsaredevelopedanApproved

FDA/CTTI CI Course

- **Conducted yearly 2009-2013**
- **May watch past presentations posted at:**
- **http://www.fda.gov/ScienceResearch/Special**