Sponsor-Investigator Responsibilities In Clinical Trials

Margaret Huber, RN, BSN, CHRC
Compliance Manager

EMORY

The lecturer has no conflicts for this presentation

Sponsor-Investigator Responsibilities

Objectives

- Define terms sponsor, investigator, and sponsor-investigator.
- Define responsibilities of sponsor, investigator, and sponsor-investigator for FDA regulated studies with regard to IND/IDE.
- Describe resources available to meet sponsor-investigator responsibilities for IND/IDE application and regulatory compliance.

Sponsor-Investigator Responsibilities

Start out right.

Know your responsibilities.

"It takes less time to do a thing right
than it does to explain why you did it wrong."
Henry Wadsworth Longfellow

Sponsor-Investigator Responsibilities

An individual may function as an investigator, sponsor, or sponsor-investigator of a clinical investigation.

Be aware of the responsibilities of each role.

Sponsor-Investigator Responsibilities

FDA defines the terms **Sponsor, Investigator** and **Sponsor-Investigator** in its regulations for investigations using drugs (21 CFR § 312.3) and devices (21 CFR § 812.3) .

The following definitions are from the drug regulations; equivalent definitions are found in the regulations for investigational devices.

Sponsor-Investigator Responsibilities

What is a sponsor?

"A **Sponsor** means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a **sponsor-investigator**."

Sponsor-Investigator Responsibilities

What is an Investigator?

"An **Investigator** means an individual who actually conducts a clinical investigation (i.e. under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. "**Subinvestigator**" includes any other individual member of that team."

Sponsor-Investigator Responsibilities

What is a Sponsor-Investigator?

"Sponsor-Investigator means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator includes both those applicable to an Investigator and a Sponsor."

Sponsor-Investigator Responsibilities

A sponsor-investigator has a
dual role and the
dual responsibilities as
defined for each:

- ✓ sponsor ***AND***
- ✓ investigator.

Sponsor-Investigator Responsibilities

CAUTION!!!

Sponsor-Investigators are responsible for:
ALL Sponsor AND ALL Investigator Responsibilities, which are described in the following slides.

Sponsor-Investigators also must be aware of FDA regulations relating to GCP and clinical trials
http://www.fda.gov/scienceresearch/specialtopics/runningclinicaltrials/ucm155713.htm

Sponsor-Investigator Responsibilities

IND and IDE

The Sponsor must:

- Determine if the investigation will require an Investigational New Drug (IND) application or Investigational Device Exemption (IDE)
- If required, submit application to FDA for investigational use.

Sponsor-Investigator Responsibilities

What is an IND?

An Investigational New Drug Application (IND) is a request to the Food and Drug Administration (FDA) to authorize the use of an investigational drug in a clinical investigation involving humans. FDA authorization is needed to be able to ship the investigational drug in interstate commerce.

An "Investigational new drug" or "investigational drug" includes (i) an unapproved drug, or (ii) an FDA-approved drug being studied, in a formal research study, for a new indication, route of administration, dosage level, subject population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the product.

Sponsor-Investigator Responsibilities

What is an IDE?

An approved Investigational Device Exemption (IDE) permits a device that does not have FDA clearance to be lawfully shipped for the purpose of conducting investigations of that device.

Sponsor-Investigator Responsibilities

When is an IND or IDE needed?

- An IND or IDE is required to move drugs and devices that have not been approved/cleared by the FDA in interstate commerce.
- In order to determine if an IND or IDE is required, consult the following FDA guidance documents:
  - IND determination for drug studies: *www.fda.gov/downloads/Drugs/Guidances/UCM229175.pdf*
  - IDE determination for medical device studies: *www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf*

Sponsor-Investigator Responsibilities

When is a study exempt from IND requirements?

- Clinical investigations that use FDA approved drugs and that meet the requirements at 21 CFR Section 312.2(b) do not require an IND.
- If an investigator believes that a study does not require an IND, but the IRB disagrees, then the sponsor will be requested to submit an IND application to the FDA to determine if an IND is required.

Sponsor-Investigator Responsibilities

When is a study exempt from IDE requirements?

- Studies that meet the requirements set forth at 21 CFR Section 812.2(c) are exempt from IDE requirements.
- Studies of non-significant risk devices are eligible for abbreviated IDE requirements. Under an abbreviated IDE, an IDE application does not need to be submitted to the FDA. Instead, the reviewing IRB has oversight for the study.
- The sponsor makes an initial determination as to whether a device is a significant or non-significant risk device. If the IRB disagrees with a sponsor's determination that a device is non-significant risk, then the FDA is consulted. The FDA has the final say regarding risk level determination.

Sponsor-Investigator Responsibilities

How do I obtain an IND or IDE?

- Develop a protocol
- Submit the following documents to FDA:
  - application Form FDA 1571 for an IND
  - application for an IDE (no form provided for IDE)
- Submission forms & templates are available at compliance.emory.edu. Email compliance@emory.edu or call (404) 727-2398 for assistance with the submission process.

Sponsor-Investigator Responsibilities

Sponsors

Sponsor-Investigator Responsibilities

Sponsors are responsible for:

- Selecting qualified investigators and monitors
- Providing information to conduct investigation properly
- Ensuring proper monitoring
- Ensuring that the investigation is conducted according to the general investigational plan and protocol
- Maintaining an effective IND or IDE
- Ensuring that the FDA and participating investigators are promptly informed of significant new information

Sponsor-Investigator Responsibilities

Selection of Qualified Investigators

Sponsors may ship the investigational drug or device only to qualified investigators.

Sponsors must obtain the following information from an investigator before permitting that investigator to begin participation in an investigation:

- Signed investigator agreement or statement (Form 1572 for IND studies) in which the investigator agrees to conduct the study in accordance with FDA requirements
- CV or statement of qualifications and experience
- Signed financial disclosure information
    - Note – The FDA financial disclosure is different from that required for participating in NIH or other PHS funded research.

Sponsor-Investigator Responsibilities

Providing information to conduct investigation properly

- A sponsor shall give investigators copies of the investigational plan (protocol) before beginning an investigation, and keep investigators informed of new observations.
- IDE sponsors must provide reports of prior investigations of the device.
- The sponsor must document protocol-specific training for all study personnel who have delegated responsibilities.

Sponsor-Investigator Responsibilities

Ensuring Proper Monitoring

The sponsor shall

- Select monitors qualified by training and experience
- Review the progress of the ongoing investigation
- Review and evaluate safety and effectiveness information.

Sponsor-Investigator Responsibilities

Ensuring that the investigation is conducted according to the general investigational plan and protocol

Sponsors must:

- Monitor the progress of all clinical investigations conducted under the IND or IDE to verify that –
    - The rights, safety, and welfare of human subjects are protected
    - The reported clinical data are “adequate and accurate”
    - The conduct of the trial is in compliance with the protocol and regulations
- Ensure investigator compliance; correct problems or terminate a site’s participation, and report terminations

Sponsor-Investigator Responsibilities

Site Monitoring is a sponsor requirement. Monitoring is mandatory, not optional.

Monitoring is required by FDA regulation . See the following sections of 21 CFR:

312.50 Responsibilities of sponsors
312.53(d) Selecting monitors
812.25(e) Monitoring procedures

Review the following guidance documents

FDA: Monitoring of Clinical Investigations
http://www.fda.gov/ora/compliance_ref/bimo/clinguid.html
ICH: E6 Good Clinical Practice
http://www.fda.gov/cder/guidance/959fnl.pdf

Sponsor-Investigator Responsibilities

Maintaining an effective IND or IDE

Sponsors must:

- Provide information necessary for the IRB to evaluate risk and benefit including any determination of IND exemption eligibility or whether a device is a significant or non-significant risk device.
- Submit safety reports to IRB and FDA.
- Submit IND or IDE annual reports to FDA.

Sponsor-Investigator Responsibilities

Keeping FDA and Investigators Informed

Sponsors must:

- Promptly provide FDA, participating investigators & IRBs with significant new information regarding adverse events or risks. Report should be identified to the FDA as IND or IDE Safety Reports.

- Promptly investigate any safety reports that are received from investigators and provide follow-up to the FDA.

Sponsor-Investigator Responsibilities

Documentation and Record Retention:

Sponsors must document that responsibilities have been met and maintain adequate study records.

The following records must be kept:

- All Correspondence with investigators, monitors, IRBs, and FDA
- Signed investigator agreement or statement (Form 1572 for IND trials)
- Financial disclosure information
- Records regarding anticipated and unanticipated adverse events or reactions
- Labeling, shipment and disposition of the investigational drug or device
- Any other records pertaining to the conduct of the study

Sponsor-Investigator Responsibilities

Sponsor record retention requirements:

- Drugs:
  - 2 years after a marketing application is approved

  OR
  - 2 years after shipment and delivery of the drug is discontinued and FDA is notified
- Devices:

  2 years after the latter
  - Date that investigation is terminated or completed

  OR
  - Date records no longer required for premarket application or completion of product development

Additional record keeping requirements for Emory at "**RETENTION SCHEDULES**" on http://records.emory.edu/

Sponsor-Investigator Responsibilities

Clinical Investigators

Sponsor-Investigator Responsibilities

Clinical Investigators are responsible for:

- Ensuring that the investigation is conducted according to the general investigational plan, protocol, and applicable regulations
- Controlling the drug or device under investigation
- Obtaining IRB approval prior to enrolling subjects and maintaining continuing approval
- Obtaining and documenting informed consent before enrolling subjects
- Reporting adverse events to the sponsor

Sponsor-Investigator Responsibilities

Following the protocol and regulations

Clinical investigators must:

- Ensure that the investigation is conducted in accordance with the current protocol and regulations.
- Ensure that all individuals assisting in conduct of the study are informed of their obligation.
- Personally conduct or supervise the investigation. Any delegation of duties must be made to qualified study personnel and documented.

Sponsor-Investigator Responsibilities

Controlling the Drug or Device under Investigation

Clinical investigators must:

- Use drug or device only in/on subjects enrolled on study
- Ensure adverse effects (AEs) are appropriately documented and reported
- Maintain adequate records of use and disposition of drug or device

Sponsor-Investigator Responsibilities

Ensuring IRB approval

Clinical investigators must:

- Obtain IRB approval prior to enrolling subjects
- Maintain continuing IRB approval
- Report any withdrawal of IRB approval to the FDA

Sponsor-Investigator Responsibilities

Informed Consent

Clinical investigators must:

- Obtain and document informed consent before enrolling subjects
- Document the consent process
- Ensure that no screening procedures are conducted prior to consent; e.g.: fasting, drug washout

Sponsor-Investigator Responsibilities

Reports

Clinical investigators must provide the following reports to sponsors, who, in turn, must retain these documents:

- Progress reports
- Adverse events
- Deviations from the investigational plan taken to protect the life or well-being of a subject in an emergency.
- Financial Disclosure reports
- Final report

Sponsor-Investigator Responsibilities

Recordkeeping and Retention

Investigators must:

- Maintain complete and accurate records of each subject's case history
- Maintain records of each subject's exposure to the drug or device including records of receipt, use, and disposition
- Maintain all correspondence with
  - –other investigators
  - –the IRB
  - –the monitor
  - –FDA

Sponsor-Investigator Responsibilities

Resources

Sponsor-Investigator Responsibilities

Emory S-I Resources

The Office of Compliance (OC) works with the S-Is and the IRB at various time points beginning with IND & IDE determinations.

Sponsor-Investigator Responsibilities

Emory S-I Resources

IND/IDE submission

- Assistance in determining which regulations apply to the research
- Education and consultation regarding regulatory requirements, compliance obligations
- Guidance and review of FDA submissions
- Review of protocol & monitoring plans prior to IRB full board review

Sponsor-Investigator Responsibilities

Emory S-I Resources

IRB Review

- When a study is identified as one having an Emory investigator as S-I, the S-I is referred by the IRB to OC for S-I training.
- S-I training includes specific regulatory requirements, compliance obligations, and best practices.
- Along with training, the S-I is requested to complete the Emory S-I IND or IDE Responsibilities Form.
- The S-I Responsibilities Form reviews required processes that must be in place and affirms that the S-I is aware of additional S-I responsibilities

Sponsor-Investigator Responsibilities

Emory S-I Resources

Ongoing support

- Development of SOPs
- Site initiation
- Continuing review
  - S-I Responsibility Form Update including compliance with DSMP
  - Amendments study sites are added or other changes to the research
  - IND communications
    - Annual reports
    - Safety reports
    - Withdrawal
  - Inspections

Sponsor-Investigator Responsibilities

Summary

Knowledge of the regulations and the responsibilities of sponsors and investigators is required to be in compliance.

Sponsor-Investigator Responsibilities

Remember these RE-SPONSOR-BILITIES!!

- Maintain IND or IDE
- Selection of investigators
- Monitor
- Control distribution and disposition of drug or device
- Maintain records
- Evaluate safety and effectiveness data
- Provide safety information to all investigators and FDA
- Ensure FDA compliance by all investigators

Sponsor-Investigator Responsibilities

Make sure that it's realistic to take on this responsibility

Ask these questions:

- Does the S-I have the time to provide appropriate oversight?
- Are there resources to do this?
  - Who will provide regulatory support?
  - Who will monitor the study?
  - Who will manage the data collection and data entry?

Sponsor-Investigator Responsibilities

Remember these important points

- Take advantage of sponsor-investigator training and site initiation assistance offered by the Office of Compliance.
- Set up systems and procedures to assist in carrying out clinical trial functions when you start a trial

Sponsor-Investigator Responsibilities

Resources

- Information on IND/IDE submissions including forms and templates:
  - compliance@emory.edu
  - mhuber@emory.edu
  - 404.727.2398
- FDA offers resources http://www.fda.gov/scienceresearch/specialtopics/runningclinicaltrials/ucm155713.htm

Sponsor-Investigator Responsibilities

References

- Guidance for Clinical Investigators, Sponsors, and IRBs: IND Applications-Determining whether Human Research can be conducted without an IND http://www.fda.gov/downloads/Drugs/Guidances/UCM229175.pdf
- FDA Regulations Relating to Good Clinical Practice and Clinical Trials http://www.fda.gov/scienceresearch/specialtopics/runningclinicaltrials/ucm155713.htm
- Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: Significant Risk and Nonsignificant Risk medical Device Studies www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf

Sponsor-Investigator Responsibilities

Questions