Clinical Investigator & Sponsor
Roles & Responsibilities for Devices

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Agenda

- **Bioresearch Monitoring (BIMO) Program**
- Drug vs Device Studies
- Definitions
- Clinical Investigator & Sponsor Responsibilities
- Common Deficiencies

BIMO Program

- FDA-wide program
- Site inspections and data audits
- Oversees FDA-regulated research
  - Significant Risk Devices
  - Non-Significant Risk Devices
  - Exempt Devices

BIMO Program Objectives

- Protect the rights, safety and welfare of subjects in FDA-regulated trials.
- Determine the accuracy and reliability of clinical trial data submitted to FDA in support of research or marketing applications.
- Assess compliance with FDA's regulations governing the conduct of clinical trials, including those for informed consent and ethical review.

BIMO Program Inspection Types

- Sponsors/Monitors/CRO's
- Institutional Review Boards
- Clinical Investigators
- Non-Clinical Laboratories

FDA Regulations for Devices

21 CFR…

- Part 50: Human Subject Protections
- Part 54: Financial Disclosure
- Part 56: Institutional Review Boards
- Part 809: In Vitro Diagnostic Products (IVD)
- Part 812: Investigational Device Exemption (IDE)
- Part 814: Premarket Approval (PMA)

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Drug vs Devices

	Drugs	Devices
# of subjects	1000's	100's
Trial Design	Phase I,II,III,IV	Feasibility, Pivotal
Blinding	Common	Difficult
CI Training	Important	Critical

Drug vs Devices

Adverse Events

Devices: investigators shall submit to the sponsor and reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation. 21 CFR 812.150(a)(1)

Drugs: investigators shall promptly report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug. 21 CFR 312.64(b)

Drug vs Devices

Adverse Events

Devices: sponsors shall report results of an evaluation of an unanticipated adverse device effect to FDA and all reviewing IRBs within 10 working days. 21 CFR 812.150(b)(1)

Drugs: sponsors shall notify FDA of any unexpected fatal or life-threatening event within 7 calendar days (IND Safety Report) 21 CFR 312.32

Drug vs Devices

Contract Research Organizations (CROs)

Device regulations

- DO NOT transfer responsibilities to CROs
- Sponsor is ultimately held responsible

Drug regulations

- Define transfer of responsibilities to CROs
- CROs are held responsible

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Significant Risk Studies

21 CFR 812.3(m)

FDA approved – IDE required

- Intended as implant
- Support/sustain human life
- Substantial importance in diagnosing, curing, mitigating, treating disease or preventing impairment of human health
- Potential of serious risk to health, safety or welfare of subject

*Uncertain in risk classification - call FDA

Non-Significant Risk Studies

21 CFR 812.2(b)

- Do not meet Significant Risk definition
- Based on indication, not just device
- Sponsor responsibilities:
  - No FDA approved required
  - IRB determines NSR vs SR
  - Comply with labeling
  - Informed consent
  - Monitor
  - Selected records and reports
  - Comply with investigational promotion & advertising

Sponsor

21 CFR 812.3(n)

Person, i.e., individual, company, gov't agency, academic institution, private organization, who

- Takes responsibility
- Initiates investigation

Clinical Investigator

21 CFR 812.3(i)

- an individual or responsible leader
- actually conducts a clinical investigation
- immediate direction
- test article administer, dispense, or use
- a research subject

Sponsor-Investigator

21 CFR 812.3(o)

- Individual, alone or with others
- initiates & actually conducts
- immediate direction
- test article
- administer, dispense, or use
- a research subject

Unanticipated Adverse Device Effect

21 CFR 812.3(s)

Any serious adverse effect on the health or safety of a subject or any life-threatening problem or death caused by or associated with the device that was not previously identified in nature, severity, or degree of incidence in the investigational plan, or any other unanticipated serious problem associated with a device

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Sponsor Responsibilities

21 CFR 812 Subparts C & G

- General Duties
- Selection of Investigators
- Monitoring
- Controlling Distribution and Disposition of Devices
- Prohibition of Promotion and Other Practices
- Supplemental Applications
- Maintaining Records
- Submitting Reports
- Inspections

Investigator Responsibilities

21 CFR 812 Subparts E & G

- General Responsibilities
- Specific Responsibilities
- Maintaining Records
- Inspections
- Submitting Reports
- Device Distribution and Tracking
- Prohibition of Promotion and Other Practices
- Annual Progress Reports and Final Reports

Sponsor-Investigator Responsibilities

All of the above

Clinical Investigator Responsibilities

21 CFR 812. 100 – General Responsibilities

- Protocol Adherence
- FDA Regulations
- Subject Rights, Safety & Welfare
- Device Control

Clinical Investigator Responsibilities

21 CFR 812. 110 – Specific

- IRB approval
  - Required prior to subject participation
  - Required prior to enrolling subjects
  - Required prior to consenting subjects
- Compliance
  - FDA regulations
  - Sponsor agreement
  - Protocol
- Device Use
  - Only used for subjects in the study
  - Only used by authorized study personnel
- Financial Disclosure

Clinical Investigator Responsibilities

Records & Reports

21 CFR 812.140(a)

- All correspondence
- Device Tracking (receipt, use, disposition)
- Subject Records
- Protocol Deviations
- Any other records required by regulation

Clinical Investigator Responsibilities

Reports to the Sponsor & IRB

Reports 21 CFR 812.150

- Unanticipated Adverse Device Effects (10 days)
- IRB approval withdrawal (5 days-sponsor only)
- Progress (yearly – monitor too)
- Deviations - emergencies (5 days)
- Device use w/o Informed Consent (5 days)
- Final Report (3 months)

Record Retention

21 CFR 812.140(d)

- Throughout the study
- 2 years after
  - Termination/completion of study; or
  - No longer needed to support PMA

  *** whichever is latest**
- Transfer custody
  - notify FDA in 10 working days after transfer
  - New custodian must comply w/retention requirements

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Common Investigator Deficiencies

- Did not follow investigational plan or FDA regs
- Did not follow signed investigator agreement
- Inadequate case history/device exposure
- Improper informed consenting
- Inadequate records

protocol/deviations
adverse effects
relevant observations
device accountability

Considerations

- Principle Investigator is ultimately responsible
  - Not delegates
  - Not study staff
  - Not clinical coordinator
- Imperative to obtain and review hospital records during course of study
- *Report findings as per protocol & regulation*

Common Sponsor Deficiencies

- Inadequate monitoring
- Record keeping
- Failure to report UADEs
- Inadequate device accountability
- Failure to obtain FDA/IRB approval

Considerations

- Select qualified study staff
- Identify and select appropriate sites
- Obtain feedback on protocol requirements
- Provide adequate training up front
  - Stress informed consent process requirements
  - Stress protocol adherence requirements
- Ensure adequate monitoring
- Bring investigators into compliance

Resources

Significant Risk vs Non-Significant Risk Devices
http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/UCM118082.pdf

Bioresearch Monitoring Internet
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/BioresearchMonitoring/default.htm

Bioresearch Monitoring Learning Modules
http://www.fda.gov/Training/CDRHLearn/ucm162015.htm

Sponsor responsibilities for significant risk devices
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm049859.htm

Investigator responsibilities for significant risk devices
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm049864.htm

Questions?

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