Institutional Review Board Responsibilities in making the Significant Risk and Non-significant Risk Device Determination

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Learning objectives

- Make distinction between significant risk (SR) and non-significant risk (NSR) device studies
- Describe three criteria IRBs should consider when making the SR/NSR determination
- Identify how IRBs document their determination

Topics

- Background
- Define SR and NSR device studies
- IRB Responsibilities
- What IRB's consider when making the SR/NSR determination
- Documentation of IRB determination

Background

- Investigational Device Exemption (IDE) Regulation is found Title 21 CFR 812
  - Sponsor and IRB responsibilities for NSR device determination
- Why provide this information?
  - Improve IRB understanding of responsibility
  - Improve compliance with FDA regulation
- IRB serves as FDA surrogate for NSR investigations
  - Initial and continuing review

What is a Significant Risk Device?

- Definition
  - Intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject
  - Purported or represented for supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject

What is a Significant Risk Device?

- Definition
  - Used for substantial importance in diagnosing, curing, mitigating, or treating disease and presents a potential for serious risk to the health, safety, or welfare of a subject
  - Otherwise presents a potential for serious risk to health, safety, or welfare of a subject
- Examples: Dental lasers, embolization devices for urological use, and collagen and bone replacements

What is a Non-Significant Risk Device?

- One that does not meet the definition of a significant risk device
- Examples: External monitors for insulin reactions, general biliary catheters, MRI within specified parameters

Who Decides Whether a Device is SR or NSR?

- Sponsors
  - Make the initial risk determination
  - Presents the IRB with this information
- IRBs
  - Required to determine whether the NSR device study involves a SR or NSR device
- FDA
  - Available to help
  - Final arbiter

What are the Requirements in 21 CFR 812 for NSR Device Studies?

- Abbreviated requirements at 21CFR 812.2(b)
  - Labeling, IRB approval, informed consent, monitoring, record keeping, reports, and prohibition against promotion.
- NSR studies are considered to have an approved IDE therefore no IDE to FDA
- Sponsors and IRBs do not have to advise FDA of NSR device studies
- IRBs must make a SR or NSR determination for every NSR study (21 CFR 812.66)

What is the sponsor's responsibility to the IRB for NSR device studies?

- Provide reviewing IRBs with a brief explanation of why the device is not a SR
- Any other information requested by the IRB
  - Description of device
  - Reports of prior investigations
  - Proposed investigational plan
  - Subject selection criteria
- Inform IRB if FDA determined the study to be NSR

What is the IRB responsibility for NSR device studies presented for review?

- IRBs should make the SR or NSR determination about a study by reviewing relevant information at a convened meeting.

What Should IRBs Consider When Making the SR or NSR Determination?

For studies presented as NSR device studies, IRBs should consider:

- What is the basis for the risk?
  - Proposed use of device
- What is nature of harm that may result from the use of the device?
- Any additional procedures?
  - Potential harm from procedures

Let's Put This into Practice

Study of a change in a component of a device. For example: new leads, battery pack, or software of an approved pacemaker

- Basis for risk: Any change to a component is a change to the device itself
- This study is significant risk and requires IDE approval by FDA

More Practice

Study of a 510k, non-significant risk, daily wear lens device to be used as overnight lens. Design changes.

- Proposed use and nature of harm: Potential for injury not normally seen with daily wear lens
- This study is significant risk and requires IDE approval by FDA

What Happens When the Sponsor and IRB Determination Disagree?

- If the IRB determines that a NSR device study involves a SR device
  - IRB must inform the clinical investigator and where appropriate the sponsor
  - The study cannot start until sponsor obtains an IDE

What Happens When the IRB Agrees with the Sponsor's NSR Determination?

- If IRB determination of NSR agrees with sponsor's NSR
  - IRB can review the study using criteria at 21 CFR 56.111
  - The study may begin without notice to FDA or IDE application to FDA

How do IRBs Document the SR or NSR Determination?

- Write determination in minutes
  - Give reason for determination
- NSR studies
  - Maintain all materials reviewed

References

- FDA Information Sheets
  - http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials
- Procedures for Handling Inquires
  - http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/BioresearchMonitoring/default.htm

Summary

- Made distinction between significant risk (SR) and non-significant risk (NSR)
- Described criteria IRB should use when making SR or NSR determination
- Described how to generate documentation of IRB's determination of SR or NSR