Conducting Clinical Research with Medical Devices

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What is an IDE?

- The purpose of an IDE submission
- Different types of IDEs
- What an IDE does/does not permit
- When should manufacturers or physicians seek an IDE
- Roles of IRBs, investigators and sponsors
- Pre-IDE submissions
Law ⇒ Regulation


– Part 812 - IDE Regulation
– Part 50 - Protection for Human Subjects, Informed Consent (IC) Regulation
– Part 54 – Financial Disclosure of Investigators
– Part 56 - Institutional Review Boards (IRBs) Regulation
Section 520(g) of the FD&C Act

Purpose of an IDE

To encourage discovery and development of useful medical devices for human use, to the extent consistent with the protection of the public health and safety and with ethical standards, while maintaining optimum freedom for scientific investigators in their pursuit of that purpose.
Purpose of an IDE

An approved Investigational Device Exemption (IDE) allows:

• an investigational device to be used in a clinical study in order to collect S&E data required to support a Premarket Approval (PMA) application, a Humanitarian Device Exemption (HDE), or a Premarket Notification [510(k)] submission to FDA.

• a device to be shipped lawfully for the purpose of conducting investigations
Provisions of the IDE Regulation

- All clinical investigations subject to the regulation must be approved before they can begin
- Assigns responsibilities to all participants in clinical investigation
- All subjects in the investigation must give informed consent
Different Types of IDEs

- Feasibility Study, Single Center
- Pivotal Study, Multi-Center
- Randomized vs. Non-Randomized
- Double Blind vs. Single Blind vs. Unblinded
- Concurrent Control vs. Historical Control
- Sponsor-Investigator Open-Label, Single Center
- Treatment Use, Multi-Center
- Continued Access, Multi-Center
- Emergency/Compassionate Use, Single Center
Approved IDEs are EXEMPT from:

- Misbranding
- Registration
- Performance Standards
- 510(k)
- PMA
- HDE

- Good Manufacturing Practices (GMPs)
- Color Additive requirements
- Banned Devices
- Restricted Device requirements
Approved IDEs are NOT EXEMPT from:

- Adulteration
- Labeling
- Prohibition on: promotion and/or marketing, commercialization, prolonging the investigation, representing the device as safe and effective
- Import/Export
Studies Subject to the Regulation

- To support marketing application [PMA, HDE or 510(k)]
- Collection of safety and effectiveness information (e.g., for a new intended use of a legally marketed device)
- Sponsor-investigator studies of unapproved devices or new intended use of approved device (even if no marketing application planned)
All Device Investigations

Studies Subject to the IDE Regulation
- SR Investigations
  - Full Requirements
- NSR Studies
  - Abbreviated Requirements

Studies Exempt from the IDE Regulation
Studies Exempt from Need for IDE

- Preamendments (pre-1976) devices
- 510(k)-cleared or PMA-approved devices, if used in accordance with approved labeling
- *In vitro* diagnostic devices (most of the time)
- Consumer preference testing
- Combinations of legally marketed devices
- Custom devices (NARROWLY defined)
“Practice of Medicine”

“Nothing in this Act shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship….”

From Section 906 of the FD&C Act
“Practice of Medicine”

• Physician should:
  – Be well informed about the product
  – Use firm scientific rationale and sound medical evidence
  – Maintain records on use and effects

• IDE not required; institution may require IRB review/approval and informed consent

• Other prohibitions still apply
“Basic Physiological Research”

- Investigating a physiological principle
- No intent to develop the device for marketing
- Only using the device to address the research question

⇨ No IDE needed; IRB approval and IC should be obtained
If NOT Exempt from Device Regulation, Then…

• Need to assess whether proposed study of device is considered **SIGNIFICANT RISK (SR), or NONSIGNIFICANT RISK (NSR)**
• IRBs can and do make this assessment most of the time
• FDA can assist IRBs and/or investigators by making risk determinations; this determination is final
Significant Risk (SR) Study

Presents a potential serious risk to the health, safety, and welfare of a subject and is:

– an implant; or
– used in supporting or sustaining human life; or
– of substantial importance in diagnosing, curing, mitigating, or treating disease or preventing impairment of human health
Significant Risk (SR) Study Examples

• Evaluation of a marketed biliary stent for use in the peripheral vasculature
• Evaluation of unapproved radiofrequency ablation device for treatment of primary hepatic neoplasia
• Extended wear contact lenses
Significant Risk IDEs

• Sponsor submits IDE application to FDA
• FDA approves, conditionally approves or disapproves IDE within 30 calendar days
• Sponsor obtains IRB approval
• After both FDA and IRB approve the investigation, study can begin
Non-Significant Risk IDEs

• Sponsor presents protocol to IRB and a statement why investigation does not pose significant risk
• If IRB approves the investigation as NSR, it can begin
• Abbreviated IDE requirements (labeling, IRB, consent, monitoring, reporting, prohibition on promotion)
• **No** IDE submission to FDA needed
Non-Significant Risk Study Examples

- Most functional MRI studies
- Study of non-invasive blood pressure measuring device
- Electroencephalography studies
- Studies of wound dressings
- Contact lens studies (daily wear only)
- Studies of conventional laparoscopes
Study Determination Inquiries

• If an IRB is uncertain whether a study is exempt, significant risk or nonsignificant risk, FDA will make a determination.

• Submit an outline/draft protocol and details about the device(s) that are being investigated as a “Pre-IDE” submission.

• FDAs will issue a letter; the determination is binding on the study sponsor and IRBs.
SPONSOR Responsibilities

• Ultimately LEGALLY responsible for:
  – IRB approval
  – Conduct and monitoring of study
  – Reporting to IRB and FDA (initial, continuing, final, unexpected AEs, study suspension, device recall, emergency use, IRB withdrawal, etc.)
  – Device disposition
  – Investigator agreements
  – Informing other investigators as needed
  – Adequate record-keeping
  – Labeling
  – Prohibition of promotion/marketing
“A sponsor is responsible for assuring, through personal contact between the monitor and each investigator, that the investigator clearly understands and accepts the obligations incurred in undertaking a clinical investigation.”

Monitoring Guidance:

http://www.fda.gov/RegulatoryInformation/Guidances/ucm126400.htm
Investigator Responsibilities

• Sign Investigator Agreement—Commit to:
  – Follow protocol, FDA regs, and IRB/FDA conditions of approval
  – Provide financial disclosure or certification to sponsor initially and updates

• Obtain IRB Approval
  – Initial, for study changes, & at least annually
Investigator Responsibilities

• Conduct Study:
  – Obtain informed consent from subjects (note: subjects are considered enrolled in the study when they sign the IC)
  – Follow protocol, collect data (fill out CRFs)
  – Submit required reports to IRB and sponsor
The IDE Pre-Submission Program

1999 Guidance:
- Goal is to benefit the sponsor
- Not a pre-requisite for an IDE
- Single cycle

Pre-IDE is appropriate:
- During testing or protocol development
- For NSR study protocols
- To determine whether a significant or non-significant risk device study
- For \textit{in vitro} diagnostic device study protocols
- Study protocols to be conducted outside U.S. (OUS)
The IDE Pre-Submission Program

Pre-IDE is not appropriate:

– If device or indications for use are not well characterized
– For an in-depth review of data
– To determine regulatory path [510(k) vs. PMA]
– To determine jurisdiction for combination products
– To determine the device classification
Resources

• Information Sheet Guidance For IRBs, Clinical Investigators, and Sponsors
  http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/ucm113709.htm
  – Frequently Asked Questions About Medical Devices
  – Significant Risk and Nonsignificant Risk Medical Device Studies

• Device Advice:
  http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm

• CDRH Learn:
  http://www.fda.gov/Training/CDRHLearn/default.htm
Questions/Comments

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