PMAs, 510(k)s, and Advanced IDE Topics

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Overview of Presentation

- Summary of 510(k) Process
- Summary of PMA Process
- IDE Risk Classification
- CMS Categorization of IDEs
- IRB Involvement in HUD Use
- IDE Approval vs. Conditional Approval
- Summary
Summary of 510(k) Process
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Summary
Summary of 510(k) Process

- 510(k) is Premarket Notification submission

- Manufacturer demonstrates their device is substantially equivalent to a currently marketed predicate device
  - Materials
  - Design
  - Technology
  - Intended use
  - Performance
510(k) Specifics

- 510(k) pathway mostly reserved for Class II devices
  - Special controls
  - Examples: Surgical instruments

- Clinical data only provided in about 10% of 510(k)s
  - 510(k)s mostly include non-clinical data

- Review time is typically 90 days or less
FDA can require post-market surveillance of 510(k)-cleared devices

- 21 CFR Section 522

Device must be either:

- Likely to have serious adverse health consequences as a result of failure
- Intended for at least one year of implantation
- Life-sustaining
Section 522 Studies

- FDA specifies type of surveillance
  - Examples: non-clinical studies, complaint review, RCT

- IRB involvement may be necessary if clinical data are collected
  - Post-market surveillance plan will include study specifics
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Summary of PMA Process

- PMA is Pre-Market Approval application

- Manufacturer demonstrates a reasonable assurance of safety and effectiveness for device based on its intended use

- No predicate device involved
PMA Specifics

- PMA process reserved for **Class III** devices
  - Highest-risk
  - Example: Pacemakers
  - All devices are Class III unless otherwise specified

- Clinical data provided in most PMA submissions

- Review time is typically 180 days or less
PMA Post-Market Issues

- FDA can require post-market studies for PMA-approved devices
  - Condition of PMA approval
  - Provided in PMA approval order (public information)

- FDA considers risks and benefits of pre-market and post-market data collection
  - Device availability vs. clinical evidence development
Post-Approval Studies

- Post-approval study conditions agreed upon by PMA sponsor and FDA

- May involve:
  - Collection of data from new patients
  - Collection of data from existing patients
  - Enhanced analysis of adverse event data

- IRBs review and approve post-approval study clinical protocols
IDE Risk Classification

From FDA’s perspective, clinical studies are either significant risk or non-significant risk.

**Significant risk devices:**
- Present a potential for serious risk to health, safety, or welfare of a subject
  - Implant
  - Life-sustaining
  - Prevents impairment of health through treatment or diagnosis

All other devices are non-significant risk.
Risk Determination

- **Study sponsor makes initial risk determination**
  - Presented to IRBs for their review
  - IRB can modify determination

- FDA may make risk determination prior to IRB review
  - IDE submission and approval
  - Risk determination request outside of IDE

- Risk determination by FDA is a binding decision
Significant Risk Studies

- Significant risk studies must follow all IDE regulations
  - 21 CFR 812

- FDA approval of IDE needed to initiate studies
  - Proof of IRB approval of study must be provided to FDA unless waiver granted
Non-Significant Risk Studies

- Non-significant risk studies must follow abbreviated IDE regulations (21 CFR 812.2(b))
  - IRB approval
  - Labeling
  - Informed consent
  - Monitoring and records
  - Prohibition against promotion

- FDA approval of IDE not necessary
What About Minimal Risk?

- Minimal risk ≠ Non-significant risk

- Minimal risk studies are non-significant risk studies that present no more than minimal risk to subjects
  - Harm and discomfort not greater than ordinarily encountered in daily life or routine medical exams

- Minimal risk studies are subject to expedited IRB review (21 CFR 56.110)
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CMS Categorization

FDA and CMS have an agreement whereby FDA provides CMS information about the investigational devices included in each IDE it approves.

Aids CMS in making “reasonable and necessary” coverage determinations for investigational devices.

Prior to this agreement, CMS reimbursement for IDE procedures was uncommon.
Experimental Devices

- Two main device classifications
  - Experimental and non-experimental

- Experimental devices have unanswered initial safety and effectiveness questions
  - Completely new device type
  - “Absolute risk” not yet established

Experimental Device ≠ Investigational Device
Category A - Experimental

A1: Class III device of a type for which no PMA has been approved for any indicated use

A2: Class III device that would be Category B (Non-Experimental) but has undergone significant modifications for a new intended use
Category B – Non-Experimental

**B1:** Device under investigation to determine substantial equivalence (510(k) expected)

**B2:** Class III device with similar technology and intended use to currently marketed device

**B3:** Class III device with technological advances compared to marketed device (next-generation)
Category B – Non-Experimental

- **B4**: Class III device comparable to marketed device under investigation for a new intended use

- **B5**: Pre-Amendments Class III device for which no PMA has been approved

- **B6**: Non-significant risk devices for which FDA requires an IDE
Categorization Information

- CMS does not reimburse for experimental devices
- Categorization determination is confidential
- Sponsor may request reconsideration
- FDA may change categorization if new information becomes available

Example: PMA for comparable device approved
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Humanitarian Use Device (HUD)

HUD intended to treat or diagnose diseases that affect fewer than 4,000 individuals per year in U.S.

HUD determination made by FDA’s Office of Orphan Products Development

HUDs can be marketed after FDA approval of Humanitarian Device Exemption (HDE)
  - Demonstrate safety and probable benefit
IRB Involvement with HDEs

- HUDs can only be used at institutions where IRBs can oversee the use of the device

- IRB must initially approve use of HUD
  - After HDE approval
  - Establish policy for HUD use
  - Informed consent not required by FDA
  - 21 CFR 56

- IRB should conduct continuing review of HUD use
  - Expedited review may be appropriate
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IDE Approval vs. Disapproval

IDE Approval – FDA has no concerns about device safety or the validity of the clinical data to be collected

IDE Disapproval – FDA has significant concerns about device safety or the scientific soundness of the proposed study that prevent initiation of the clinical study
IDE Conditional Approval

- FDA may conditionally approve an IDE if there are outstanding questions regarding the device or the proposed study that do not involve device safety.

- Sponsor must respond to FDA’s concerns within 45 days.

- IRBs may contact FDA if they have general questions about conditional approval decisions – FDA cannot comment on specific IDEs because of confidentiality requirements.
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Device marketing submissions are either PMA or 510(k) depending on risk classification and controls. IRBs can be involved in pre-market study and post-market surveillance review process regardless of whether device is marketed via 510(k) or PMA.

Sponsors make initial risk significance determination. IRB reviews this determination. FDA decision is final.
Summary (2)

- CMS categorization based on knowledge of device risks or lack thereof
  - Category letter (A or B) more important than number

- IRBs responsible for oversight of HUD use

- IDE conditional approval means that there are no outstanding safety concerns with device
  - Study can initiate while sponsor addresses concerns
Additional Information

- FDA has numerous guidance documents available that IRBs may find helpful
  - Frequently Asked Questions about IRB Review of Medical Devices
  - Significant Risk and Non-significant Risk Medical Device Studies
Questions About…

- IDEs/HDEs?
- PMAs?
- 510(k)s?

Contact IDE, PMA, or 510(k) Staff at:

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Questions About Presentation?

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