

# PMA's, 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

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# 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

# 510(k) Post-Market Issues

- 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

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# 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  $\neq$  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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# Summary (1)

- 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
  - <http://www.fda.gov/oc/ohrt/irbs/irbreview.pdf>
- Significant Risk and Non-significant Risk Medical Device Studies
  - <http://www.fda.gov/oc/ohrt/irbs/devrisk.pdf>



# Questions About...

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

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

(240) 276-4040



# Questions About Presentation?

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