Statutory Framework for Devices

Medical Devices

- Investigational Use Application
  - IDE (21 CFR 812)
  - Abbreviated IDE
  - Exempt

- Pre-Market Approval Applications
  - §510(k) Pre-marketing Notification (21 CFR 807(e))
    - Class II (general & special controls)
  - §515 Premarket Approval Application (PMA) (21 CFR 814)
    - Class III (special controls insufficient)
    - Exempt
    - Class I (general controls)
Basic Device Requirements

- Establishment registration (21 CFR 807)
- Medical device listing (21 CFR 807)
- Quality System Regulation (QS) (21 CFR 820)
- Labeling is not False and Misleading (21 CFR 801)
- Medical Device Adverse Event Reporting (21 CFR Part 803)
Medical Device Classification

- Medical device classification is based on the level of control necessary to assure the safety and efficacy of the device (risk-based paradigm)

- Class I
  - Common, low-risk devices
  - General controls (§513(a)(1) of FD&C Act)
  - Exempt: no premarket 510(k) submission
  - Non-exempt: premarket 510(k) required
Medical Device Classification

- **Class II**
  - more complex, higher risk, defined class effect
  - General controls and special controls (§513(a)(1)(B) of the FD&C Act)
  - Exempt: no premarket 510(k) submission
  - Non-exempt: premarket 510(k) required

- **Class III**
  - Most complex, highest risk, no class effect;
    - Supports or sustains human life
    - Use is substantially important in preventing impairment of human health
    - Presents unreasonable risk of illness or injury.
  - General controls and
  - Pre-market approval (PMA) application (515 FD&C Act) required
Medical Device Classification

- Find regulation number:
  - Over 1,700 types of devices classified
  - FDA’s classification database;
  - Device panel/medical specialty (21 CFR 862-892)
    - Contains list of devices within that panel

- Each classified device has 7-digit number associated with it (e.g., 21 CFR 880.2920)

- 7-Digit Classification citation will described Class and controls
  - Online search provides 3-digit product code (find predicates this way)
Investigational Device Exemption (IDE)

- Allows investigational device to be used in clinical study in order to collect safety and effectiveness data required to support 510(k) or PMA.
  - Most clinical studies support PMA; small percentage conducted for 510(k)

- IDE exempts product from compliance with
  - Most QSR, registration, listing and 510(k) or PMA

- IDE required for all investigational devices unless
  - Exemption applies
IDE

Types of IDEs:

- IDE for Significant Risk Device Study
  - presents a potential for serious risk to the health, safety, or welfare of a subject
  - Requires IRB approval and FDA IDE filing

- Abbreviated IDE for Non-significant Risk Device Study
  - do not pose a significant risk to the human subjects
  - Required IRB approval (21 CFR 50/56) only; no IDE submission to FDA required
  - Required to comply with abbreviated IDE requirements.
IDE

- Types of IDEs (cont.):
  - Exempt
    - Exemption categories at 21 CFR 812.2(c) (e.g., animal device, custom device, consumer preference testing, diagnostic device that is non-invasive or require an invasive sampling procedure and is not used in diagnosis w/out confirmation)
    - Still must comply w/ 21 CFR 50 and 56 re: human subject protections
  - IDE considered cleared 30 days after submission unless FDA specifies otherwise.
  - FDAMA pre-IDE meeting available (use it!).
§515 Pre-market Approval Application (PMA)

- §515 of the FD&C Act requires PMA for Class III devices
  - General and specific controls are insufficient to provide adequate directions to ensure safe and effective use of the medical device.
- Most stringent device marketing application required by FDA.
- Analogous to the §505(b)(1) of drugs and the §351(a) BLA for biologics.
- Clinical Data almost always required.
§515 Pre-market Approval Application (PMA)

- PMA data requirements for submission (21 CFR 814.20)
  - Non-clinical Laboratory Studies
    - GLP Compliant (21 CFR 58)
    - Microbiology, toxicology, immunology, biocompatibility, stress, wear, shelf life, and other laboratory or animal tests
  - Clinical Investigations
    - Study protocols
    - Safety and effectiveness data
    - Patient information and complaints
    - AERs and failures
    - Statistical analysis

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§515 PMA

Types of PMA Submissions

- New PMA
  - New indication or modification has new clinical effects (new data)
- Panel-Track Supplement
  - Change in indication or significant change in design or performance; new data is necessary, but not full battery.
- 180-Day or “Traditional” Supplement
  - “significant changes to device”; bridge data required but old data generally sufficient; changes in principal operation, control, new feature, design, labeling, manufacturing site.
- PMA Supplement – Manufacturing Site Change
  - Change in manufacturer location; usually a 180-day supplement but if site has inspection w/in last 2 years, use this approach.
§515 PMA

Types of PMA Submissions (cont.)

- Special PMA Supplement for CBE (changes being effected)
  - Labeling and manufacturing changes that enhance safety and effectiveness; “additive”
  - New safety info, strengthen warning or add contra indication
- 30-Day Notice
  - Change in manufacturing procedure; gives 30 days prior notice (may require a 135 day supplement)
- 30 Day Supplements
  - Advisory opinion issued to industry, 30 days to make change, rare
- Product Development Protocol
  - For well-established technology, matures clinical development w/ device review (like a SPA in drug paradigm)
- Annual Reports
  - Due on anniversary date of PMA approval; New Data; AERS
§510(k) Premarket Notification

- 510(k) is premarket submission to FDA to demonstrate that the device to be marketed substantially equivalent to a predicate device (21 CFR 807.92(a)(3))

- 510(k) required for Class I-III devices where
  - PMA is not required
  - No exemption applies
  - Device exceeds a limitation at exemptions listed at 21 CFR 862.9 and 864.9
§510(k) Premarket Notification

- “Predicate” device
  - Legally marketed device against which the investigational device is compared.
  - Can be a recent 510(k) cleared device

- “Substantial Equivalence”
  - New device is “at least as safe and effective” as the predicate device.
  - Compared to predicate, has same intended use and technological characteristics (or changes raise no question of safety and effectiveness).
§510(k) Premarket Notification

- Device may not be marked without letter from FDA declaring substantial equivalence.
- If “substantial equivalence” not found (“NSE”), sponsor may:
  - Resubmit 510(k) with additional data
  - Request Class I or II designation via de novo review
    - ***new de novo process under FDASIA of 2012; no NSE needed before requesting de novo review.
  - File reclassification
  - Submit a PMA

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§510(k) Premarket Notification

“New 510(k) Paradigm” 3 Types:

- Traditional 510(k)
- Special 510(k): Device Modification
  - device modifications (and submitted as a modification)
  - relying on design controls (21 CFR 820.30) by a declaration of conformation and not additional data; or verification/validation data
  - Not for changes in intended use or altering fundamental technology of the device.
- Abbreviated 510(k)
  - Applicant articulates conformation to a new guidance document on special controls, relevant special control standard, or FDA recognized consensus standard
Other Device Issues

- Custom Devices
- In Vitro Diagnostics
  - Test specimen from body; can be Class I – III
  - General purpose reagents vs. analyte specific reagents
  - CLIA standards for clinical laboratory tests
- Companion Diagnostics
  - Used on conjunction w/ therapeutic developed contemporaneously
- Combination Products
  - Regulated based on “primary mode of action”
Humanitarian Device Exemption (HDE)

- Humanitarian Use Device (HUD) (32 CFR 814.100 et seq.)
  - Device intended to benefit patients by treating or diagnosing a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year.

- Requires HDE Application to FDA
  - Similar to PMA, but no effectiveness data required
  - Sufficient information for showing no unreasonable or significant risk of illness or injury, and that the probable benefit outweighs the risk from its use, taking into account alternative forms of treatment
  - Must be administered under supervision of IRB
  - Label must explain effectiveness not demonstrated
A §513(g) “Request for Submission” may be made to request the FDA’s opinion regarding whether a product is a “device” within the meaning of §201(h) of the FD&C Act.

A §513(g) Request is less burdensome than filing a 510(k).

MDUFA Fees apply.