Regulatory Submission Strategies and Outlines For Ultrasonic Surgical Devices: Contact and HIFU Systems

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Regulation Governing Medical Devices

- Europe: Council Directive 93/42/EEC
  Medical Devices Directive

- United States: Food and Drug Act

Requirements to Legally Market Device in EU

- Europe: Must meet all of the Essential Requirements of the MDD, including
  - Evaluation of Clinical Data – Annex X and MEDEV 2.7.1
  - Notified Body Sign Off for Class III devices
  - Self certification possible for Class II devices if product category is listed on EN 13458 certification to Annex I

Requirements to Legally Market Devices in United States

- **Section 510, paragraph k of Food and Drug Act**

"(k) Each person who is required to register under this section and who proposes to begin the introduction or delivery for introduction into interstate commerce for commercial distribution of a device intended for human use shall, at least **ninety days** before making such introduction or delivery, report to the Secretary or person who is accredited under section 523(a) (in such form and manner as the Secretary shall by regulation prescribe)—

- (1) the class in which the device is classified under section 513 or if such person determines that the device is not classified under such section, a statement of that determination and the basis for such person's determination that the device is or is not so classified, and
- (2) action taken by such person to comply with requirements under section 514 or 515 which are applicable to the device."

Regulations Defining Report Required under Section 510(k)

- 21 CFR* 807 Subpart E

* Code of Federal Regulations

Where are Classifications for Specific Devices Listed

- 21 CFR Parts 862 - 892

Classes of Medical Devices

- Class I – Simplest devices:
  - Some Powered
  - Most are manual devices; i.e. brushes, trocars, forceps, roungers
- Class II – Most powered medical products such as RF devices, Cryogenic devices and Ultrasonic Surgical Aspirators
- Class III – Devices requiring Pre Market Approval under IDE/PMA guidelines unless the FDA has listed a 510k process for device

FDA Speak

- Devices which the FDA examines through the 510k process are deemed to be "CLEARED" TO MARKET
- Devices which require an IDE/PMA route are "APPROVED" to Market

- DO NOT CONFUSE THE TWO!!

Basic Goals of a 510k Submission

- Prove that the device in question is substantially equivalent to a device which was on the market before the enactment of the Food and Drug Act of 1976

Or

- Prove that the device is substantially equivalent to a device which already has a 510k Clearance letter (Predicate Device)

Types of Ultrasound Based Medical Devices

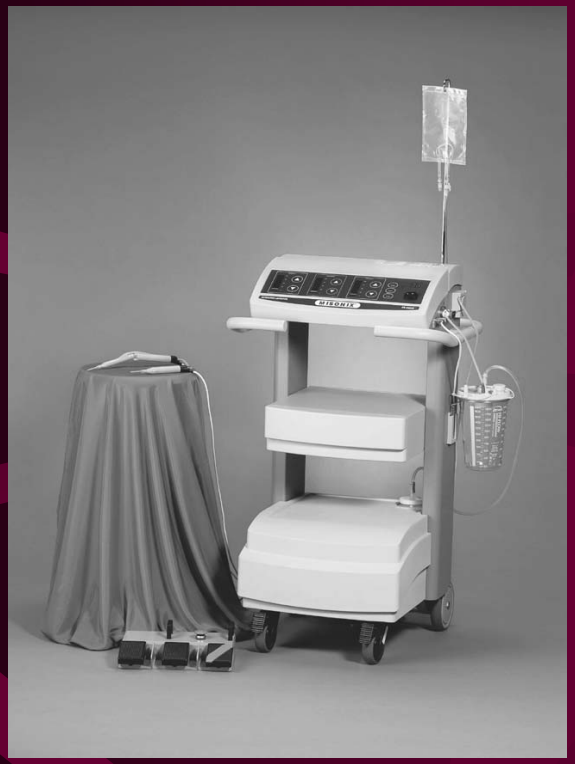
- Diagnostic Image Scanners
- Doppler Flow Meters
- Nebulizers
- Ultrasonic Diathermy Machines
- Wound or Osteo Treatment Systems
- Ultrasonic Surgical Aspirators
- HIFU Surgical Systems

- All Require PreMarket Approval by the FDA

Ultrasonic Surgical Systems and Classifications

- Contact Type Systems
  - CUSA Ultrasonic NeuroAspirator
  - LySonix or Vaser Ultrasonic Liposuction Systems
  - AutoSonix or Harmonic Scalpel Laproscopic Systems
  - Exogen Bone Healing System
- All of these systems are Class II
  - 510k Route can be used

Typical Class II Ultrasonic Medical Devices



General Purpose Ultrasonic Surgical Device Stand Alone System with Analog Control

- Neuroaspirator
  - Integrated System with Software Control

Outline of 510k Submission for a Typical Contact Ultrasonic Surgical Device

- 510(k) Cover Letter
- Truthful and Accuracy Statement
- Indications for Use Statement
- Financial Certification or Disclosure Statement (where clinicals are required)
- Device Description and Comparison to Predicate Device(s)
- 510k Summary
- Substantial Equivalency Table
- Predicate Device Information (Catalogs, 510k Summaries, etc)
- Proposed Labeling: Manuals, Advertisements, Device Labels, Packaging, etc.
- Sterilization and Shelf/Use Life Statements and Testing
- Risk Analysis
- Biocompatibility Statements or Validations
- Software Descriptions and Validations
- Electromagnetic Compatibility and Electrical Safety Certificates of Conformity
- Description of Clinical Testing or History – Bench, Animal or Clinical

Elements of 510k Which Must Describe Ultrasound Device Specifically

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Cover Letter

- Must contain required sections
  - Type of 510k, i.e. Traditional or Special
  - Common Name of Device (i.e. Ultrasonic Surgical Aspirator)
  - 510k Submitter (Who will own 510k)
  - Classification Identifier (as per FDA) or Unclassified, i.e. LFL for Aspirators
  - Contact Person Info (could be outside consultant)
  - Class of Product, I, II or III
  - Which Panel you wish to review it (suggestion only)

Cover Letter (con't)

- Reason for Submission
  - New Device
  - Major Modification
  - New Indication for Use
  - New Control Method (Microprocessor vs. Analog)
  - Minor Change (in case of Special 510k)
- Indications for Use

Cover Letter (con't)

- Design and Testing Descriptions
  - Mini Summary of 510k
    - Things to Include
      - Non Clinical Tests Performed (EMC, Hardware Tests, etc)
      - Voluntary Standards Met (UL, EN, AAMI)
      - Sterile or Non Sterile Supply
      - Software Validations or No Software Provided
      - Submission based upon results of Clinical Testing?
      - Statement of Substantial Equivalency

Indications for Use

- Must be the same as predicate devices unless clinicals are included for additional indications

Or

- Indications are omitted from 510k which are listed in the predicate

Device Description and Comparison to Predicate Device(s)

- This is the most important section of the 510k
  - Section in which you will describe your product and its similarity and differences to a product which has already achieved Market Clearance from the FDA
  - Consists of many sub elements and paragraphs where your argument will be made

Device Description and Comparison to Predicate Device(s)

- Predicate Device must be chosen carefully
  - Closer to the new product the better
  - Indications must cover intended use of device either by surgical specialty or actual procedure
    - Examples
      - General Surgery or Plastic and Reconstructive Surgery
      - Ablation of Cardiac Tissue for Atrial Fibrillation Therapy

Device Description and Comparison to Predicate Device(s)

- Predicate devices do not necessarily have to be the same technology if results and safety with new device can be proven to be substantially equivalent
  - Example
    - Magnetostrictive and Piezoelectric devices have been considered by the FDA to be equivalent even though technology of hand piece and control circuitry are different

Examples of Predicates

- CUSA Ultrasonic Surgical Aspirator
- Ultracision Harmonic Scalpel
- Integra Medical Systems
- Sound Surgical Vaser
- FibraSonics Phacoemulsifier

Device Description and Comparison to Predicate Device(s)

- Section also includes expanded descriptions of information contained in Cover Letter and Summary

Device Description and Comparison to Predicate Device(s)

- Includes:
  - Mode of Operation
  - Description of Functional Components
    - Generator
    - Handpiece
    - Accessories
  - Conformance to Voluntary Standards
  - Summary with Statement that product is substantially equivalent to predicates and introduces no new concerns of safety and efficacy

510k Summary

- Outline of 510k which will be published
- Similar to Cover Letter in Scope
- More details required
- Examples may be found in CDRH Database on Releasable 510k's

Substantial Equivalency Table

- Comparison of New Device to Predicates in Tabular Format
  - Important Parameters for Ultrasonic Devices
    - Frequency of Output Signal
    - Waveform Type; continuous wave or pulsed output
    - Output Power; Average, Maximum
    - Output Amplitude of Probes
    - Transducer Type

Substantial Equivalency Table

- Additional Important Parameters for Ultrasonic Devices

  - Irrigation Rates
  - Aspiration Rates and Pressures
  - Input Power Requirements
  - Controls (hand, footswitch, parameters)
  - Indicators and Alarms
  - Sterilization Methods
  - Materials of Construction

Labeling

- All written material regarding product
  - Instruction Manuals
  - Advertising (If developed)
  - Labels on Product and Packaging
- Drafts of Labeling generally acceptable

Validations

- Software Validations (if applicable) Complete and Performed to Appropriate Standards
- Hardware Validations – Lists of tests performed
  - Life Testing
  - Hardware Performance Testing
  - Electrical Safety Testing

Voluntary Consensus Standards

- Third party performance, safety or EMC standards recognized by the FDA
  - Third Party Examples:
    - Underwriter's Laboratories
    - IEC
    - ANSI
    - Association for the Advancement of Medical Instrumentation (AAMI)
    - NEMA

Voluntary Consensus Standards

- UL 601-1 and Collateral Standards
- IEC 60601-1 and Collateral Standards
- IEC 60601-1-2:2001 EMC Standards
- AAMI ES-1

Conformance to Consensus Standards Statement

- Since most submissions are filed before final product testing, statement that product will meet applicable Voluntary Standards is sufficient.
- Specific information is required on statement. Can be found at:

  www.fda.gov/cdrh/ode/reqrecstand.html

FDA Guidance Documents

- FDA documents which outline special controls on performance and test requirements for specific devices or indications. For Instance:
  - Information for Manufacturers Seeking Marketing Clearance of Diagnostic Ultrasound Systems and Transducers
  - Low Energy Ultrasound Wound Cleaner: Class II Special Controls Guidance Document - Guidance for Industry and FDA Staff

Evaluation of Clinical Data

- Clinical Data could be:
  - Non Human in vivo testing
  - Limited human testing done under IRB's
  - Compilation of published articles in peer reviewed journals, including those of competitors
- Non Clinical Data:
  - Bench testing done on cadaver or animal tissue

Evaluation of Clinical Data

- Report should be written which compiles all data and speaks directly to clinical safety and efficacy
- Provide very specific information on adverse events or side effects of treatment
- Compare reports on Predicate Devices to the results obtained with the new device

Risk Analysis

- Provide very detailed Risk Analysis
- Risk Analysis may be based on;
  - Fault Tree Analysis
  - EN/ISO 14973:2000 Risk Analysis

Special or Abbreviated 510k

- Used for cases where small changes in specifications are made
  - Changing Frequency of Operation (20khz to 40 kHz)
  - Change in materials of construction
- Cannot be used for:
- Adding Indications for Use
- Changes in Control Type (Analog to Digital Frequency Control)
- Increasing power output

Biocompatibility

- All materials in direct or indirect contact with patient must be USP Class VI or better
  - Biocompatibility Statement must be sent with 510k
  - Provide test data or manufacturers statement for all materials
  - Best way is to use materials which already have been referenced in other 510k's

Conclusion

- Most contact Ultrasonic Devices may be cleared through the 510k process.
- Careful consideration of Predicates and logical, complete description of device operation, safety and efficacy are required for best chance quick, positive consideration by FDA