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

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• 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, rongeurs

• 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

- Neuroaspirator
  - Integrated System with Software Control

General Purpose Ultrasonic Surgical Device Stand Alone System with Analog 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 clinics 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