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Medical Device Series

Venture Capital, IPO Markets and FDA

The 510(k) Program and FDA's Initiatives

Tips for Medical Device Companies
Direct from the FDA: Support for FDA-Regulated Firms

June 15, 2011

Boston, MA

Overview

- 510(k) Associated Activities Over the Past 18 Months
- Some Key FDA Actions/Proposals
- Premarket Notification/Substantial Equivalence (SE)?

FDA Program Perceptions

- FDA states 510(k) Program has 2 public health goals
  - Facilitating innovation
  - Assuring devices are safe and effective
- CDRH reviewer concerns
  - Fails to adapt to increasing complexity of devices
  - Reviewers' ability to make well-informed decisions undermined by poor quality of 510(k) submissions
  - Increasing workload
- Industry concerns
  - Program less predictable, consistent and transparent
  - Stifling innovation and sending companies and jobs OUS
  - CDRH reviewers less responsive and more risk averse
- Consumer groups and some healthcare professional groups concerns
  - Believe that for higher risk devices, does not provide adequate assurances of S and E
  - Results in insufficient information for providers and patients to make well-informed treatment or diagnostic decisions

510(k) Working Group and Task Force on the Utilization of Science in Regulatory Decision Making

- September 2009: CDRH convened 2 internal working groups
  - To evaluate the 510(k) process
  - To determine how CDRH can quickly incorporate new science, including evolving information, novel technologies, and new scientific methods, into its decision making
- August 2010: Preliminary reports of findings and recommendations issued for comment
- January 2011: CDRH will implement or reach a major implementation milestone for recommendations that received support
  - 7 recommendations for IOM study
  - 4 recommendations FDA is considering

IOM Study

- September 23, 2009: FDA commissioned Institute of Medicine (IOM) to "study the premarket notification program used to review and clear certain medical devices marketed in the United States"
- The IOM:
  - Not-for-profit, non-governmental organization
  - Chartered as part of the National Academy of Sciences to provide national advice related to biomedical science, medicine, and health

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IOM Study

- Two principal questions:
  - Does the current 510(k) process optimally protect patients and promote innovation in support of public health?
  - If not, what legislative, regulatory, or administrative changes are recommended to achieve the goals of the 510(k) process?

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IOM Study

- Principal substantive question is based on false premises
  - Principally, 510(k) was not intended to be the method to optimally protect patients
  - 510(k) was not intended to foster innovation
  - 510(k) was intended to sort devices into groups that would be subject to regulatory controls that would provide the right level of protection to achieve reasonable assurance of safety and effectiveness
- IOM report expected in mid-2011
  - Draft report circulated for peer review

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Congressional Oversight

- Letters to Commissioner Hamburg
  - May 25, 2010: Sen. Klobuchar and Rep. Paulsen (MN)
  - Aug. 2, 2010: House Energy and Commerce Cmte's Rep. Barton and Rep. Burgess
  - Sept. 23, 2010: 11 House members from PA
  - Oct. 12, 2010: 12 members of Energy and Commerce – bipartisan letter
    - Welcome commitment made by Dr. Hamburg in August 4, 2010 briefing to focus on recommendations with consensus
    - Identify 5 controversial proposals: rescission authority, split and multiple predicates, intended use and indications for use, premarket inspections, and clinical information for a subset of class 2 devices
  - Nov. 24, 2010: 2 Senators and 6 Reps from MN
  - Dec. 8, 2010: 15 Senators – bipartisan letter
  - Dec. 21, 2010: 9 Senators (8 R, 1 Ind.) from HELP Committee
  - Jan. 7, 2011: Sen. Lugar (IN)
  - April 13, 2011: Sen. Kerry (MA)
    - IOM panel does not include industry reps therefore urges FDA to establish a deliberative and transparent process for reviewing IOM recommendations that ensures input from all stakeholder groups

What is a Premarket Notification?

- Practically: The way most non-510(k) exempt devices get to market; 97-98% of new devices reach the market through the 510(k) process
- Legally: A method of classifying post-1976 devices
  - Demonstration of "substantial equivalence" of your device to a similar legally marketed device, *i.e.,* a "predicate" device (FDCA § 513(f)(1))
- A 510(k) is NOT a PMA or an approval; misbranding to call a 510(k) clearance an approval
- SE findings result in market "clearances" because there are no regulatory impediments prohibiting distribution

Substantial Equivalence (SE)

- FDCA § 513(i) – New device is SE if it has:
  - Same intended use as a predicate device; and
  - Same technological characteristics, or different technological characteristics and information submitted demonstrates that the device is as safe and effective as a legally marketed device and does not raise different questions of safety and effectiveness.
    - Different technological characteristics = significant change in materials, design, energy source, or other features
    - Any information requested by FDA to demonstrate SE must be related only to SE and constitute "least burdensome" means of demonstrating SE

(Cont'd)

Substantial Equivalence (SE)

- **FDA Action:** Draft guidance on 510(k) Paradigm by Sept. 30, 2011
  - To include the criteria for identifying "different questions of safety and effectiveness" and technological changes that generally raise such questions and the characteristics that should be included in the concept of "intended use"
  - To resolve discrepancies between the 510(k) flowchart and the FD&C Act
- **FDA Action**: To train CDRH staff and industry on (1) the determination of "intended use" and (2) the determination of whether a 510(k) raises "different questions of safety and effectiveness"
- **FDA Referral to IOM:** To consolidate the concepts of "indication for use" and "intended use" into a single term "intended use"
- **FDA Referral to IOM:** To explore the possibility of pursuing a statutory amendment that would provide the agency with the express authority to consider an off-label use when determining the "intended use" of a device
- **FDA Referral to IOM:** To clarify when a device should no longer be available for use as a predicate

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510(k) Content and Format

- Proposed labels, labeling, and advertising sufficient to describe the device, its intended use, and directions for use
  - **FDA Action:** Draft guidance on the 510(k) Paradigm by Sept. 30, 2011 regarding the submission of photos or schematics for internal FDA use only
  - **FDA Public Meeting (April 7, 2011):** To make device photos available in a public database without disclosing proprietary information and to develop an online labeling repository
    - Similar to labeling repository for drugs through DailyMed on National Library of Medicine?
  - **FDA Referral to IOM:** To consider the possibility of requiring each 510(k) submitter to keep at least one unit of the device under review available for CDRH to access upon request

510(k) Content and Format

- 510(k) Summary or Statement
  - **FDA Action:** Draft guidance on the 510(k) Paradigm by Sept. 30, 2011 to provide greater clarity on the development of 510(k) summaries to assure they are accurate and include all the required information
- Clinical Data
  - **FDA Action:** Draft guidance on the 510(k) Paradigm by Sept. 30, 2011 to provide greater clarity when clinical data should be submitted
  - **FDA Action:** Draft guidance by July 31, 2011 to improve the quality and performance of clinical trials
- **FDA considering** issuing device specific guidance
  - When and what type of manufacturing data to submit
  - When a pre-clearance inspection would be conducted

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510(k) Process and Review

- **FDA Referral to IOM:** To seek greater authorities to require postmarket surveillance studies as a condition of clearance for certain devices
- Administrative Appeal = 21 CFR § 10.75
  - **FDA Action:** Draft guidance by Oct. 31, 2011 to clarify the process for appealing CDRH decisions, including a decision to rescind a 510(k)
- **FDA Referral to IOM:** To consider defining the scope and grounds for the exercise of CDRH's authority to fully or partially rescind a 510(k) clearance
- **FDA Action:** Issue a Proposed Regulation by Dec. 31, 2011 regarding 510(k) transfers of ownership

De Novo Classification

- FDCA § 513(f)(2); also referred to as risk-based classification
  - If found NSE, within 30 days can request initial classification of the device into Class I or II
  - Need to describe device and provide detailed information and reasons for the recommended classification
  - FDA has 60 days to classify the device
  - Device classified through de novo process may be used as 510(k) predicate
  - If device remains in Class III, it is deemed adulterated, unless subject to PMA approval or IDE exemption, and may not be marketed
- **FDA Action:** Draft guidance by Sept. 30, 2011 to streamline the de novo process

510(k) Device Modifications

- **FDA Action:** Draft guidance by June 15, 2011 to clarify what changes trigger a new 510(k)

- **FDA considering** issuing a device-specific guidance regarding when and what types of modifications should be periodically reported in lieu of submitting a 510(k)

Additional FDA Actions/Proposals

- Establish "Notice to Industry Letters" as a standard practice
  - To clarify and more quickly inform stakeholders when CDRH has changed its regulatory expectations on the basis of new scientific information
  - To post SOP to FDA website by June 15, 2011
- **FDA Referral to IOM**: Establishment of a Class IIb
  - To develop guidance defining Class IIb devices for which clinical information, manufacturing information or, potentially, additional evaluation in the postmarket setting would typically be necessary to support a substantial equivalence determination

Questions?

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New England District

Medical Device Series

June 15, 2011

Boston, MA


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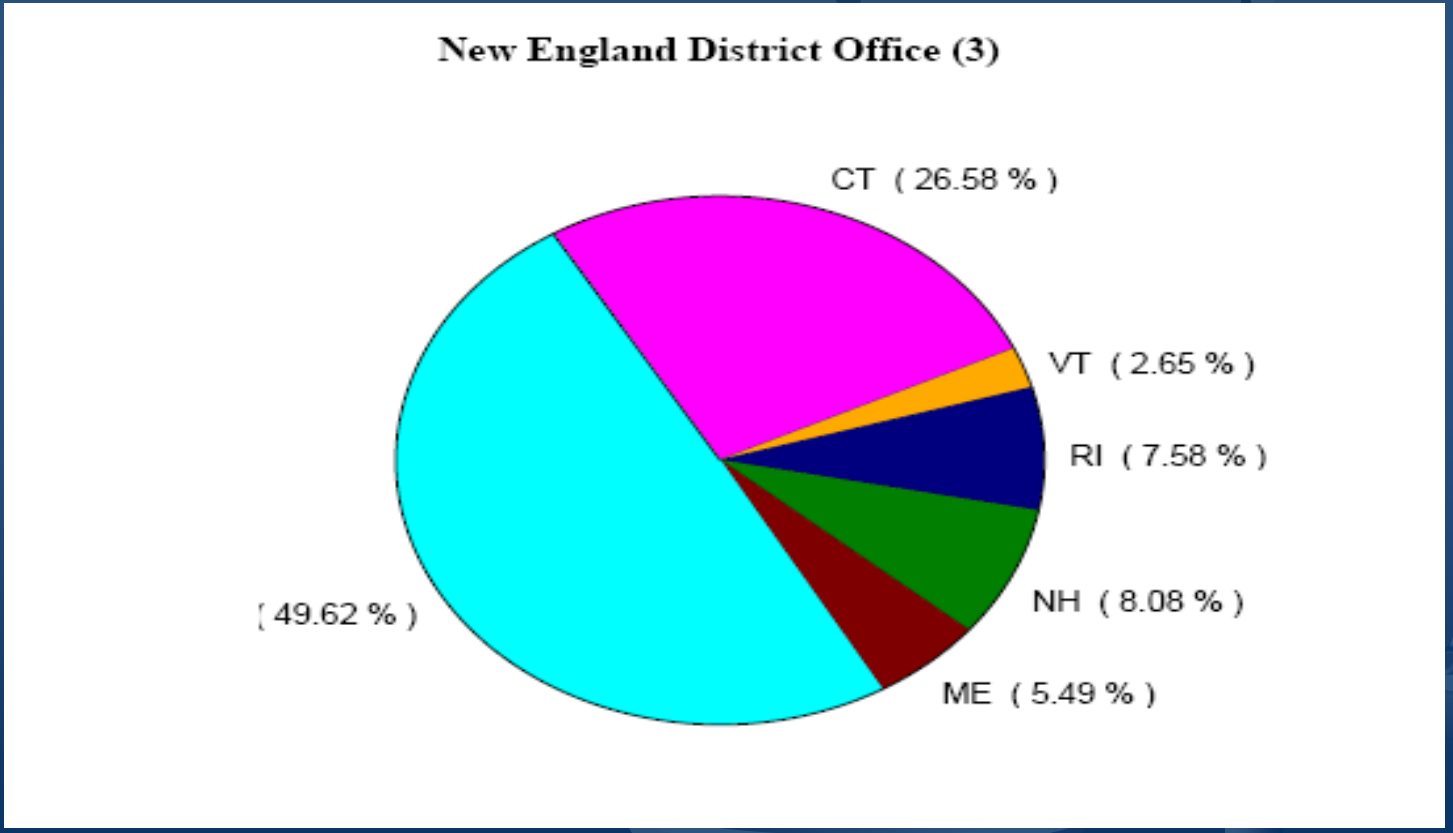
Montpelier
VERMONT
Rutland
Lebanon
Concord
Manchester
Keene
Lowell
Worcester
Providence
Hartford
New Haven
Norwich

Inventory

- 8745 establishments
  - 3021 device firms



Accomplishments FY10

- 1355 Inspections
  - 264 Device inspections
    - 20 Foreign inspections

NWE-DO Structure

- Investigations Branch
  - 108 Investigators
  - 11 Supervisors
- Compliance Branch
  - 9 Compliance Officers
- Administrative Branch

Compliance Actions

- FY10
  - 22 Warning Letters
    - 9 Device QSRs
  - 2 Permanent Injunctions
- FY11
  - 20 Warning Letters
    - 5 Device QSR's (inc 510(k) & MDR)

Commissioner's Enforcement Initiatives August 6 2009

- Implement a formal Warning Letter "close-out" process
  - After FDA determines violations have been corrected notice will be posted on FDA website
  - For WL issued after 9/1/09
- Warning Letter "close-out" process
  - Since 09/01/09 18 close out letters sent, 4 of which were device related

Transparency Initiative

- An agency-wide effort to open the doors of the agency and promote innovation, in a manner compatible with the agency goal of appropriately protecting confidential information.
- http://www.fda.gov/AboutFDA/Transparency/TransparencyInitiative/ucm254426.htm

FY10 Top Device Cites

- Lack of Written MDR Procedures
- Lack of or inadequate CAPA procedures
- CAPA Documentation
- Lack of or inadequate process validation
- Complaint handling procedures

In My Experience

- Prepare
- FDCA, CFR, IOM, RPM, CPGM, CPG, QSIT
- Inspection expectations
- Open, honest discussion
- Clear, concise response