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BOSTON MEDTECH ADVISORS

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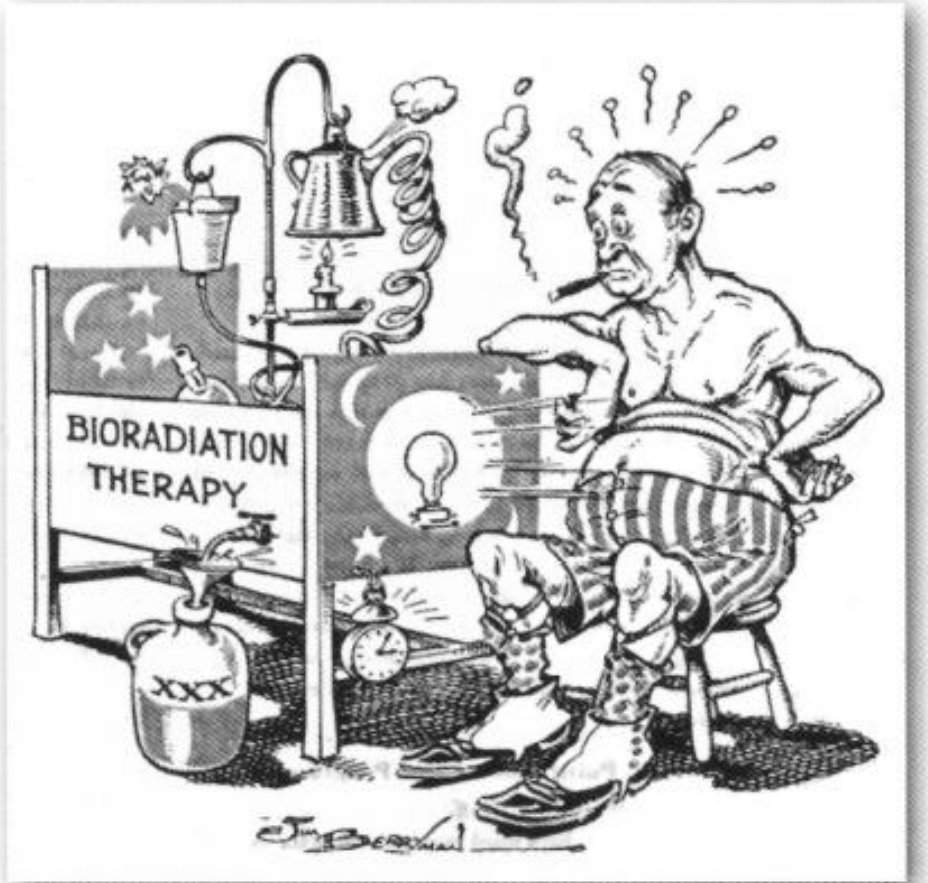
Shifting Ground in US Medical Device Regulation – Has the 510(k) Program Run Its Course?

FDA Enforcement – Pre- 1976 Amendment

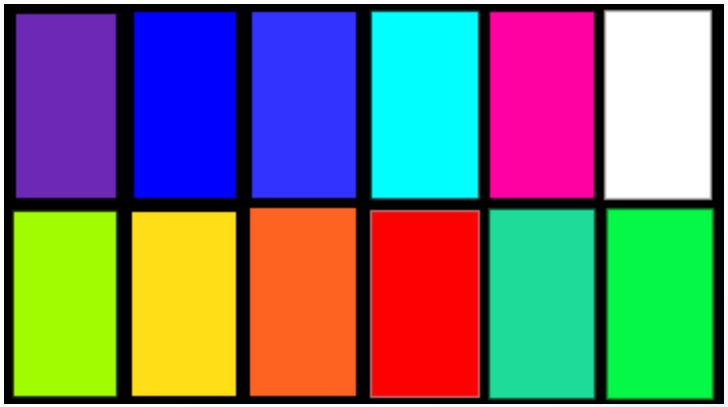
- Dinshah Ghadiali's Sectrochrome Lawsuit – 1946
  - 1000W light bulb
  - Light passes through glass tank of water
  - Crude lens focused light through colored glass slides
  - Promised
    - No diagnosis
    - No drugs
    - No manipulation
    - No surgery
  - Claim
    - "For the measurement and restoration of the human radioactive and radio-emanative equilibrium"
- Longest FDA trial – 42 days
  - Testimony showed that Ghadiali did not believe in device
  - Convicted on 12 counts on January 7 1947

Bioradiation Therapy (Quackery after WWII)

Following World War II, a surplus of electronic parts found their way on the market as bogus medical devices—which FDA prosecuted. *Look* magazine's Washington correspondent, Jack Wilson, summarized the case cartooned here as follows: "The way it works, you sit in front of the screen and turn on the lights, which glow greenly at your stomach while the smell of the herbs wafts onto your person. This is bio-radiation and you must not keep it up longer than half an hour at a stretch or you will get so young and healthy that the draft board will be after you. This is because the herbs are young herbs, it says in the book, and all you need to do to get young yourself is let them radiate at you. The machine will cure anemia, asthma, constipation, diabetes, epilepsy, goiter, high and low blood pressure, spider bites, tuberculosis, and worms, to mention a few. It is wonderful for loss of memory and leukemia, and better yet for gangrene and gland disorders. You could buy one for $240 if the FDA weren't so nasty about it, and set yourself up as a medicine man to do mankind good. But good." *Look*, October 9, 1951, p. 116.



The Spectrochrome – for the Treatment of Diabetes, Cancer, Tuberculosis and Syphilis



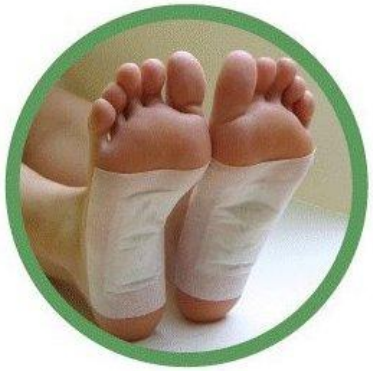
- $45

Classical spectrochrome therapy has a wealth of instruction, most notably found in the textbook of application *Let There Be Light* by the Dinshah Health Society.

The colors you see here only approximate the actual colors of the tiles. These color tiles don't require a projector or a darkened room. Complete descriptions for doing "color tonations" comes with glass. They generate 3 different types of tonating: spectrochrome, light therapy, tonating substances, and chakra work. **Instructions included.**

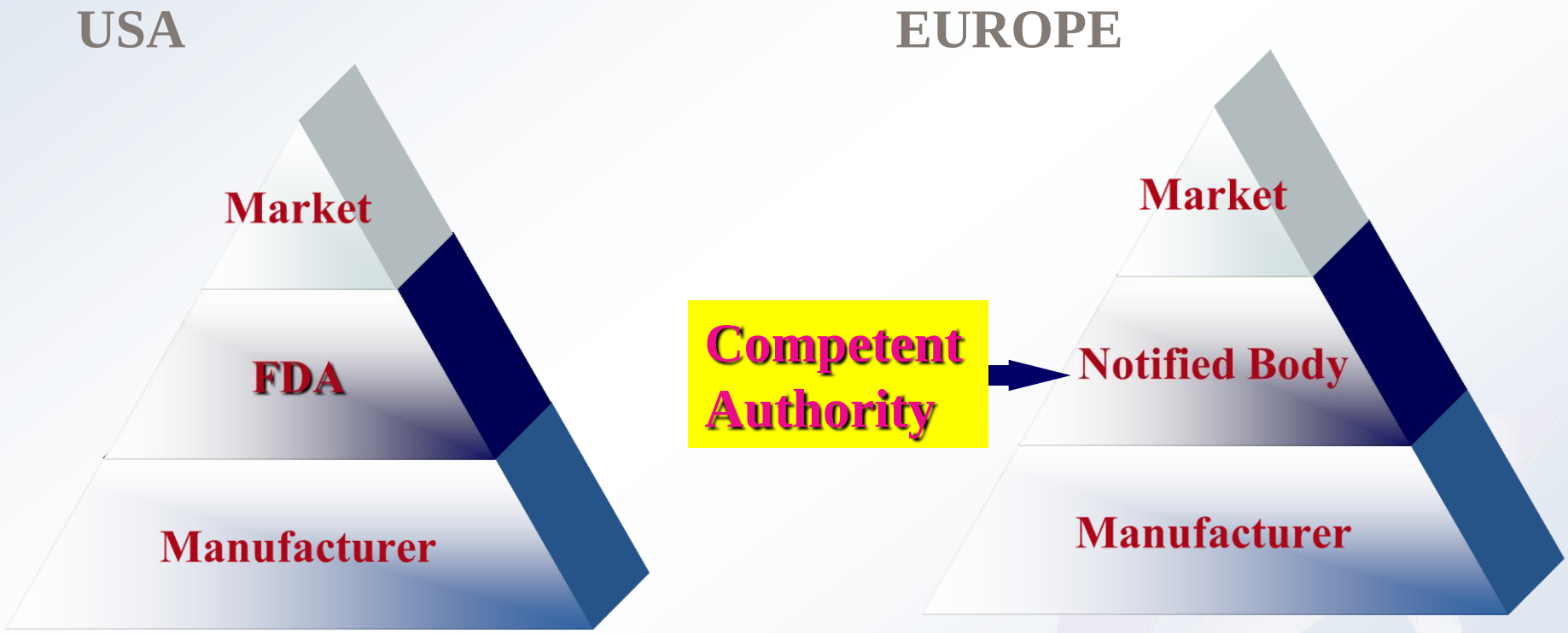
To get a copy of *Let there Be Light*, contact the Dinshah folks at...

Detox Foot Pads



- All Natural BodyRelief Detox Pain Relief Patches are reported as helpful by customers who experience:
- Aches, Sore Muscles, Numbness, Neuropathy, Pain, Swelling, Circulation Problems, Toxins, Sore Throat, Fever,
- Cough, Joint pain, Bruises, Injuries, Sore Muscles, Sinus Infections, Skin Conditions.

Regulatory Interactions



Food and Drug Administration Regulation of Medical Devices

- 1938 – Food, Drugs and Cosmetics Act
  - Through 1960 – keep ‘quack’ devices off market
  - Rely on physicians to identify ‘problem’ devices
- 1960’s – Protect patients from new, complicated devices
  - Testing
  - Manufacturing
  - Usage
- Eliminate the need to litigate every unsafe or ineffective product (Spectrochrome)

Amendments of the 1938 FDC

- 1960's
  - Social reform movement – protections of environment, civil liberties and public health
  - 1,500 manufacturers; $2B annual shipments
  - FDA lacks authority to request pre-market safety review
- 1976 Amendment
- 1990 – Safe Medical Devices Act
- 1992 – Medical Device Amendment
- 1997 – FDA Modernization Act
- 2002 –Medical Device User Fee & Modernization Act
- 2007 – Amendments of MDUFMA

Risk Based Classification of Medical Devices

USA

- Class I – General Controls
- Class II – Special Controls
  - (Class IIb? – clinical and/or manufacturing)
- Class III – Premarket Approval

Europe

- Class I – Self Certification
- Class IIa – Quality System Assessment
- Class IIb – Quality System Certification
- Class III – Product + QS Certification

1976 Amendment of the 1938 FDC

- ‘Grandfathering’ ‘pre-amendment’ devices
  - Vast majority – safe and effective
- Establishment of expert panels
- Classification of medical devices
- 19 panels working 15 years (1973-88) classified ~8,000 ‘pre-amendment’ devices
- Premarket review of medical devices
- New devices – automatic ‘Class III’ unless
  - Substantially equivalent to another device
  - Are classified by the FDA as Class I or II

Class I Devices – General Controls Requirement

- No requirement for regulatory submission (typically)
- Good Manufacturing Practices (GMP)
- Prohibit adulteration, misbranding
- Establishment registration
- Banning certain devices
- Notification of risk, replacement, repair, refund
- Sale and distribution restrictions
- Record keeping

Class III Devices – Premarket Approval

- Longest (and most expensive) process
- Typically involves three levels of testing:
  - Laboratory (technical specifications)
  - Animal
  - Human
- Typically involves panel review

Class II Devices – Premarket Notification

- Special Controls requirement
  - Performance Standards
    - Example – Intramedullary Nail
      - **ASTM standard adopted by FDA**
        - Provides lab testing information

- The 510(k) process
  - Concept of Substantial Equivalence
    - Indications for Use
    - Technological principles

1997 – FDAMA (FDA Modernization Act)

- Special 510(k)
  - No change in:
    - Intended use
    - Fundamental scientific technology
  - Adherence to Design Controls
    - Risk analysis
    - Verification and validation
      - Design outputs ⟷ Design inputs

- Abbreviated 510(k)
  - Guidance document exists
  - Special controls or accepted consensus standard
  - Compliance with standards

- De Novo Submission
  - Low risk devices
  - No predicate

- "Least Burdensome"

The De Novo Process – In Theory

Step	Sponsor	FDA	Time Frame	Comments
I	Submit 510(k) for new device			No predicate device exists
II		Review 510(k) and issue NSE[5] letter for no predicate		• No review time specified • Device is automatically designated as Class III
III	Request for Evaluation of Automatic Class III Designation submitted		30 days	
IV		Review and issue order establishing classification	60 days	FDA can either leave Class III designation, or reclassify as Class I or Class II
V		Publish finding in Federal Register	30 days	

The De Novo Process – In Practice

The Initial 510(k) Review

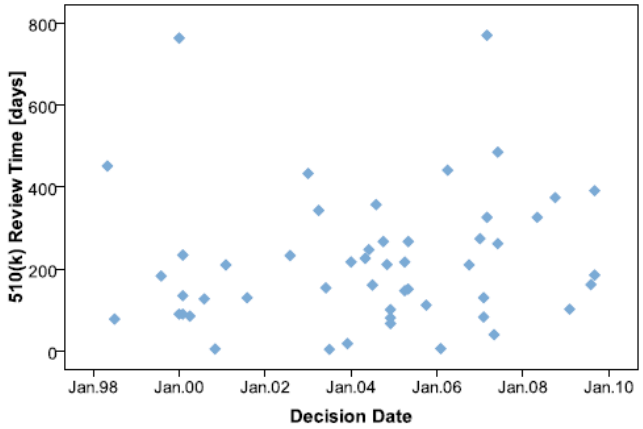


Figure 1a. Review times (days) of the 510(k) phase (Step II in Table 1).

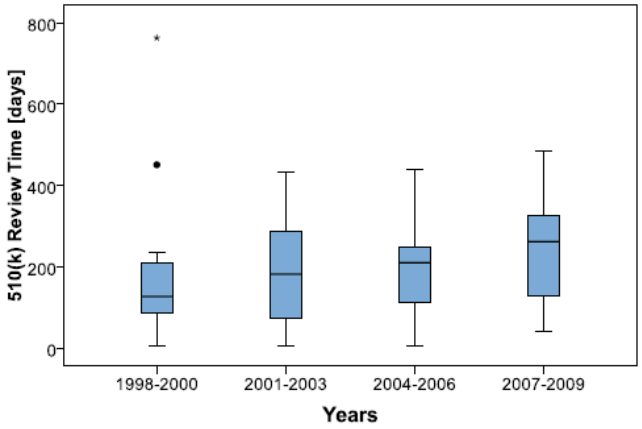


Figure 1b. Review times (days) of the 510(k) phase (Step II in Table 1). Boxplot. Boxes show first to third quartile. Line within box indicates median. Whiskers show high/low. Circles denote outliers, asterisks denote extremes.

The De Novo Process – In Practice

De Novo Review

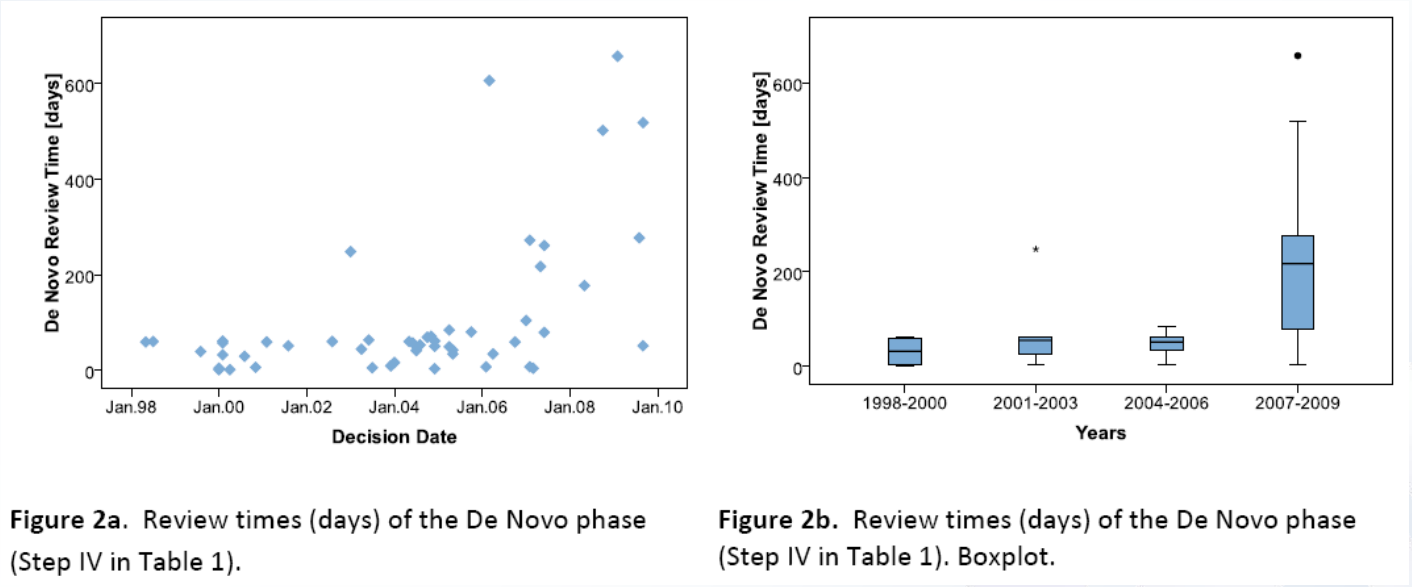


Figure 2a. Review times (days) of the De Novo phase (Step IV in Table 1).

Figure 2b. Review times (days) of the De Novo phase (Step IV in Table 1). Boxplot.

The De Novo Process – In Practice

Total Review Time

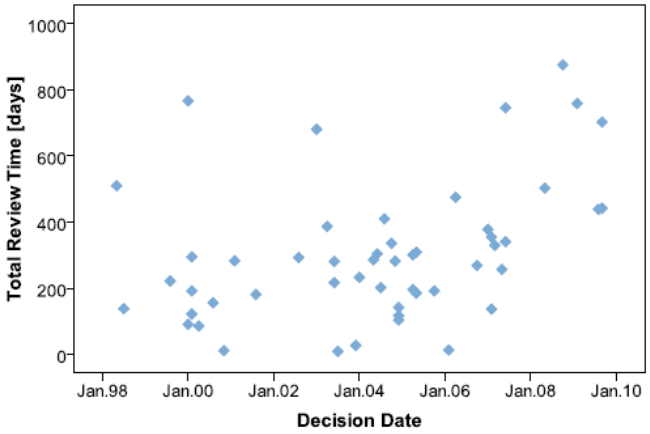


Figure 3a. Duration of total review times of De Novo products (Step II + Step IV in Table 1).

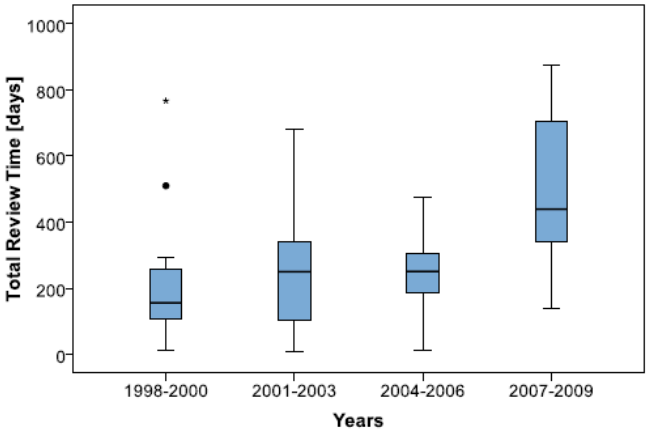
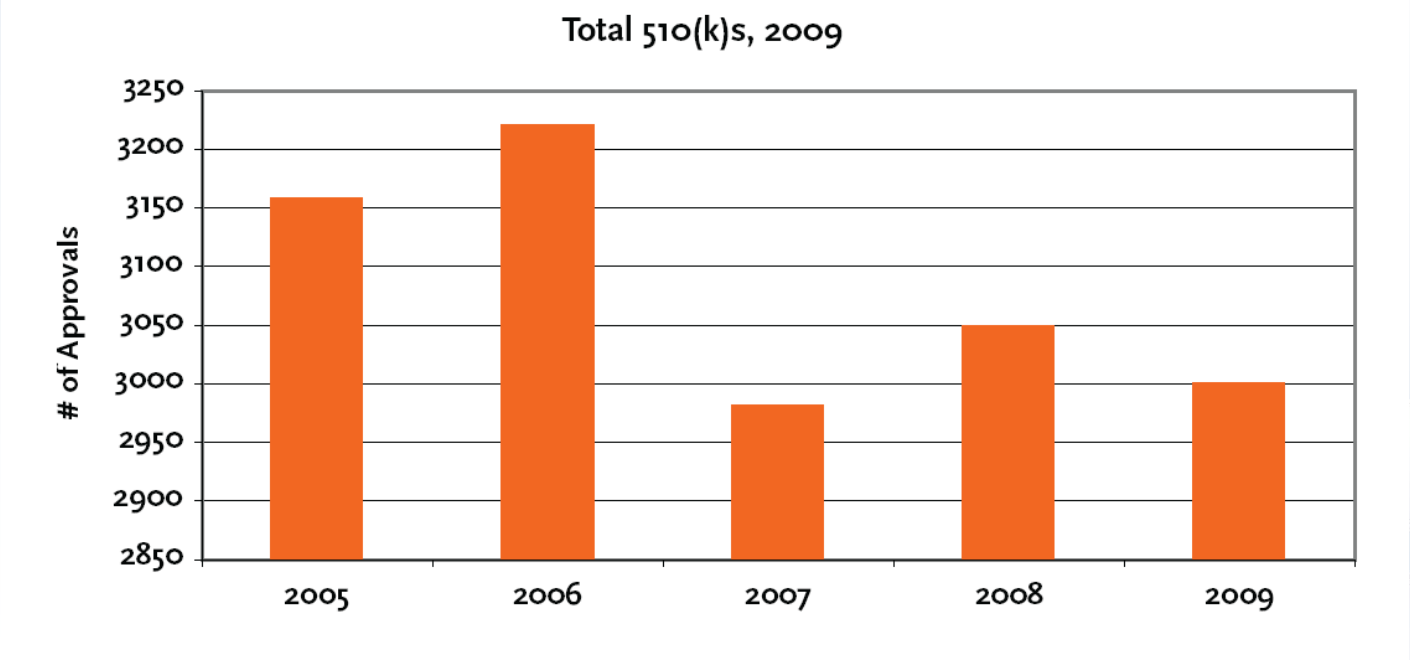


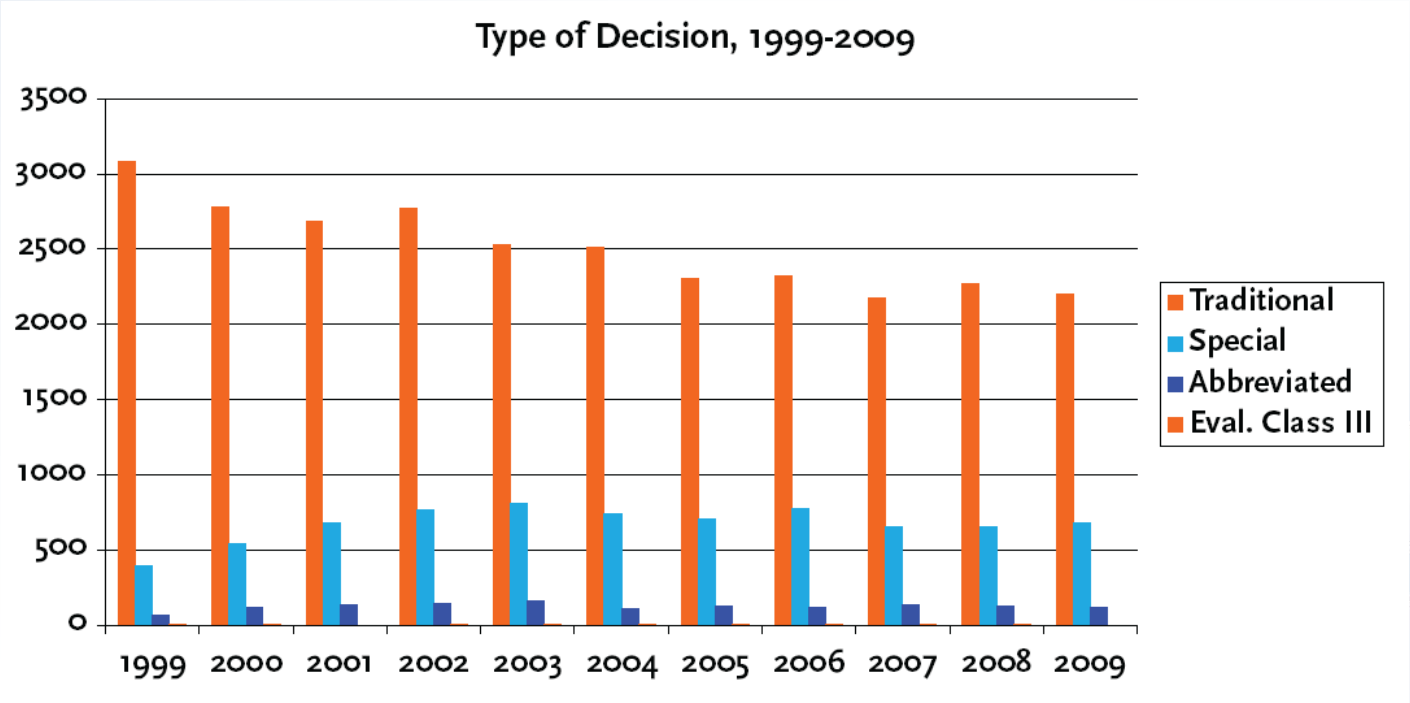
Figure 3b. Duration of total review times of De Novo products (Step II + Step IV in Table 1). Boxplot.

Cleared Medical Devices



MassDevice. Eye on FDA 2009. Massachusetts Medical Devices Journal, LLC, 2009.

Distribution of 510(k) Submissions

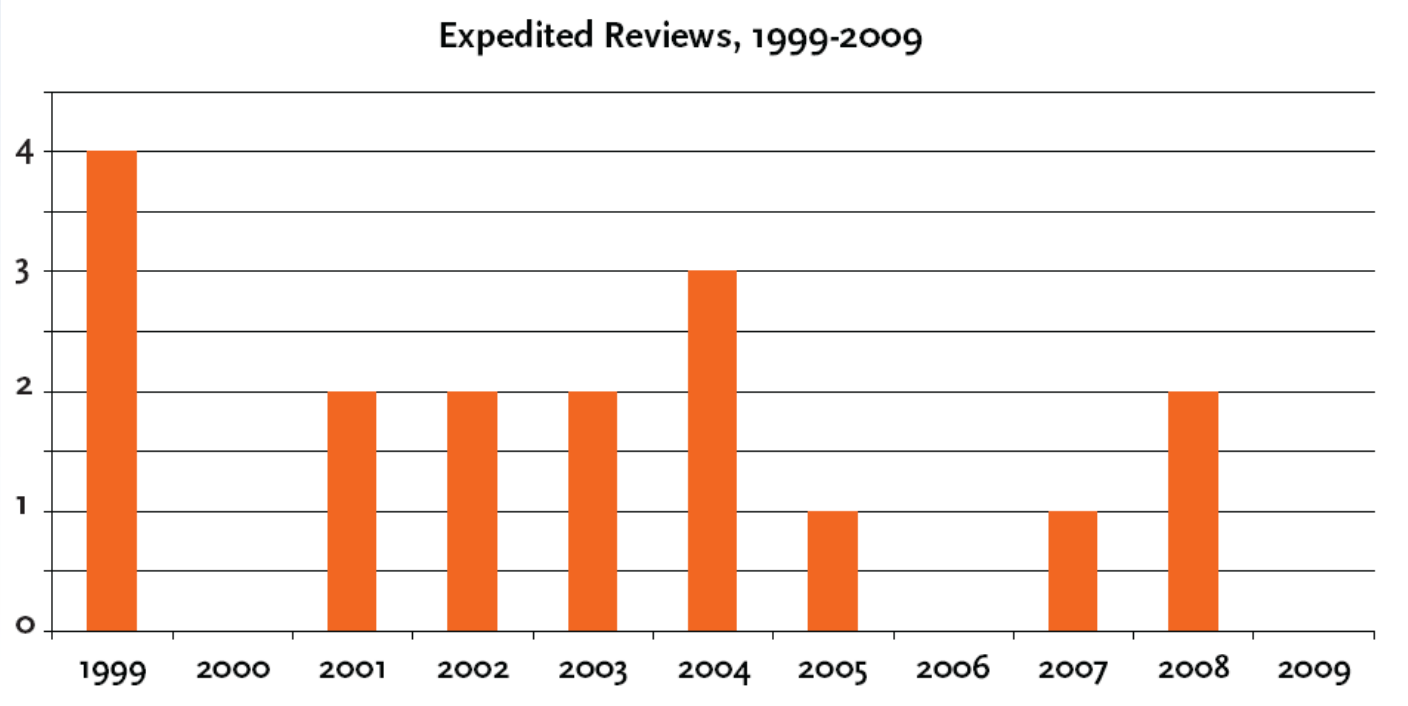


MassDevice. Eye on FDA 2009. Massachusetts Medical Devices Journal, LLC, 2009.

2007 Amendment

- Expedited Review
  - Intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition
  - Address an unmet medical need
    - Device availability is in the best interest of patients
    - No approved alternative treatment or means of diagnosis exists
  - Breakthrough technology
    - Clinically meaningful advantages over existing technologies
    - Offer significant, clinically meaningful advantages over existing approved alternative treatments

Expedited 510(k)



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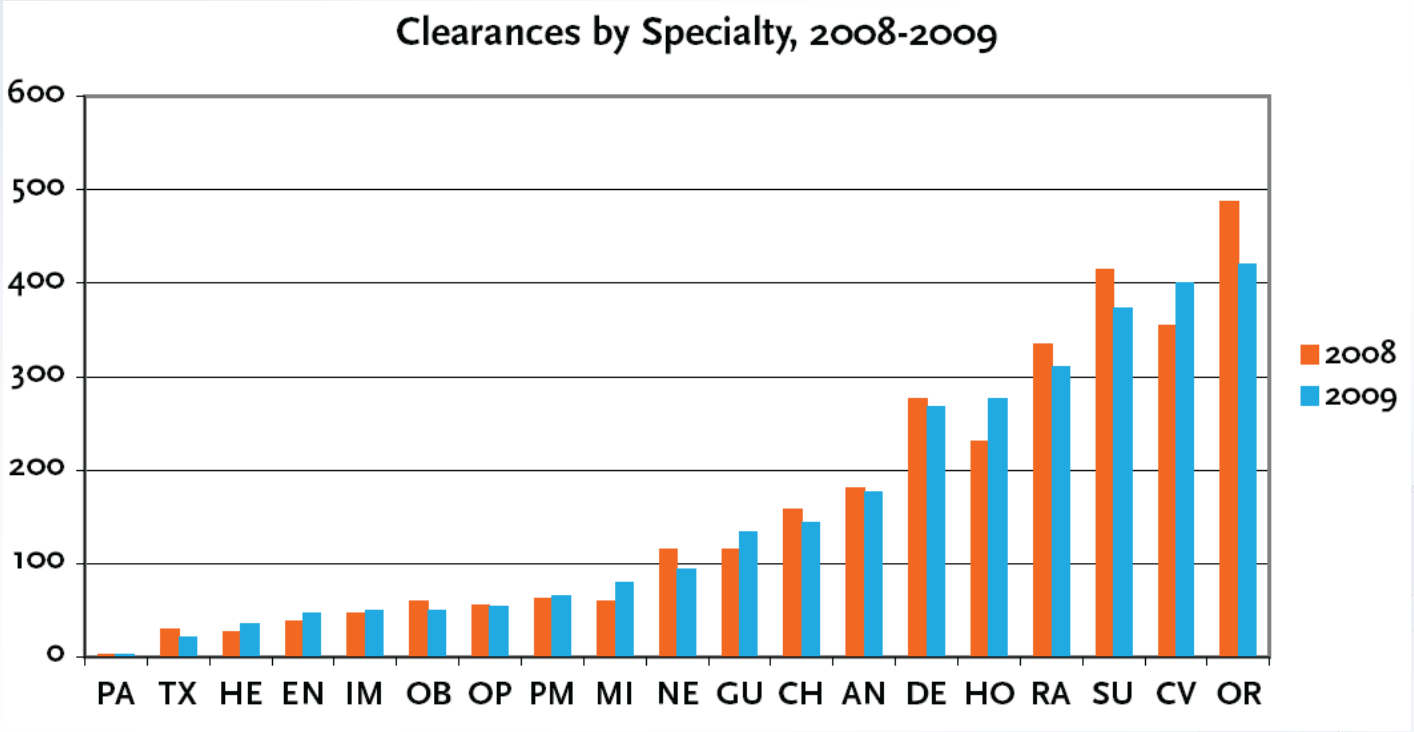
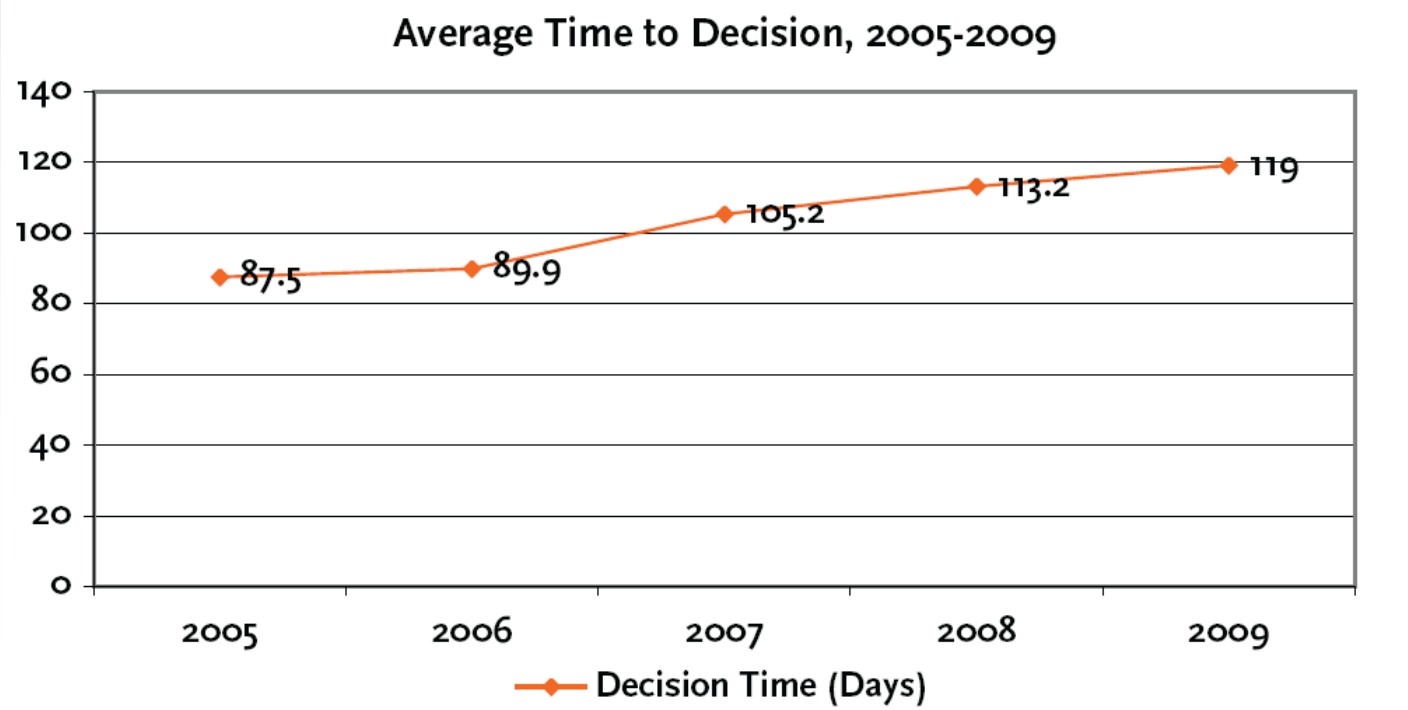
Clearances by Specialty



FDA discipline codes	
Anesthesiology	AN
Cardiovascular	CV
Clinical Chemistry	CH
Dental	DE
Ear, Nose, & Throat	EN
Gastroenterology & Urology	GU
General Hospital	HO
Hematology	HE
Immunology	IM
Microbiology	MI
Neurology	NE
Obstetrics/Gynecology	OB
Ophthalmic	OP
Orthopedic	OR
Pathology	PA
Physical Medicine	PM
Radiology	RA
General & Plastic Surgery	SU
Clinical Toxicology	TX

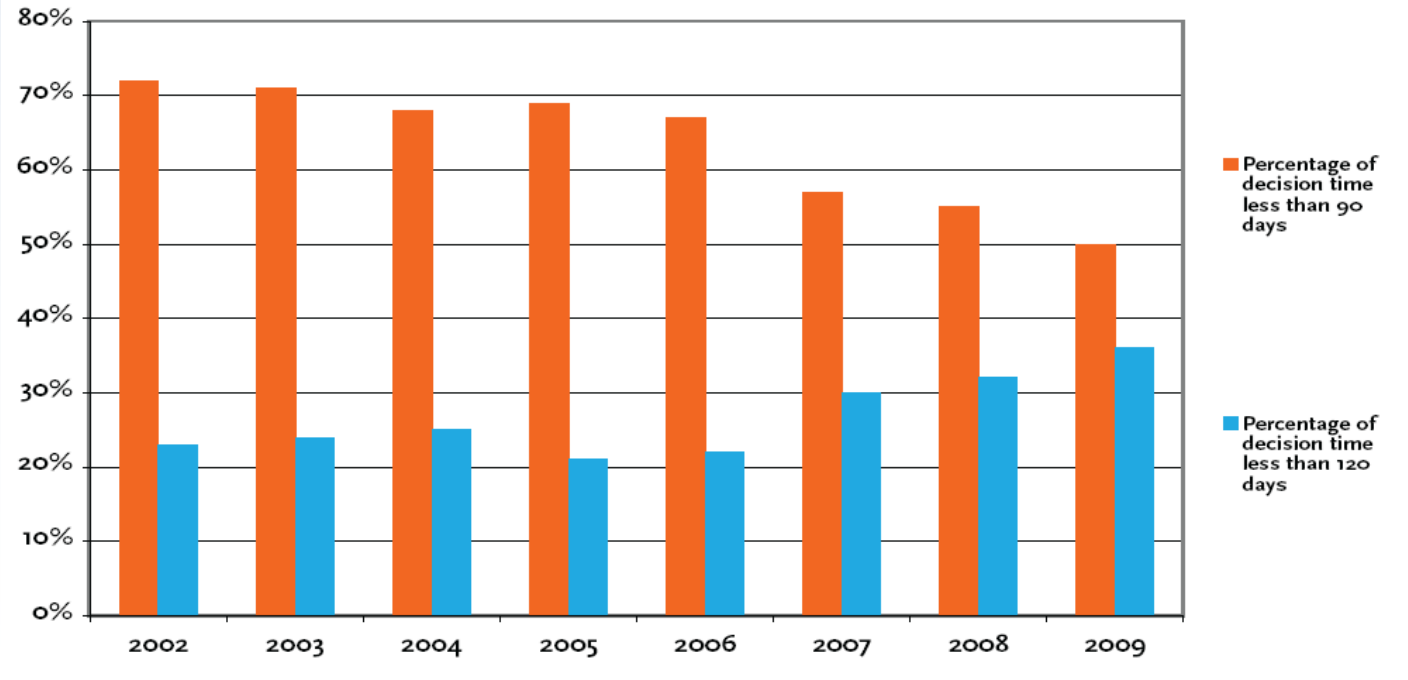
MassDevice. Eye on FDA 2009. Massachusetts Medical Devices Journal, LLC, 2009.

510(k) Review Times – Pressure Source



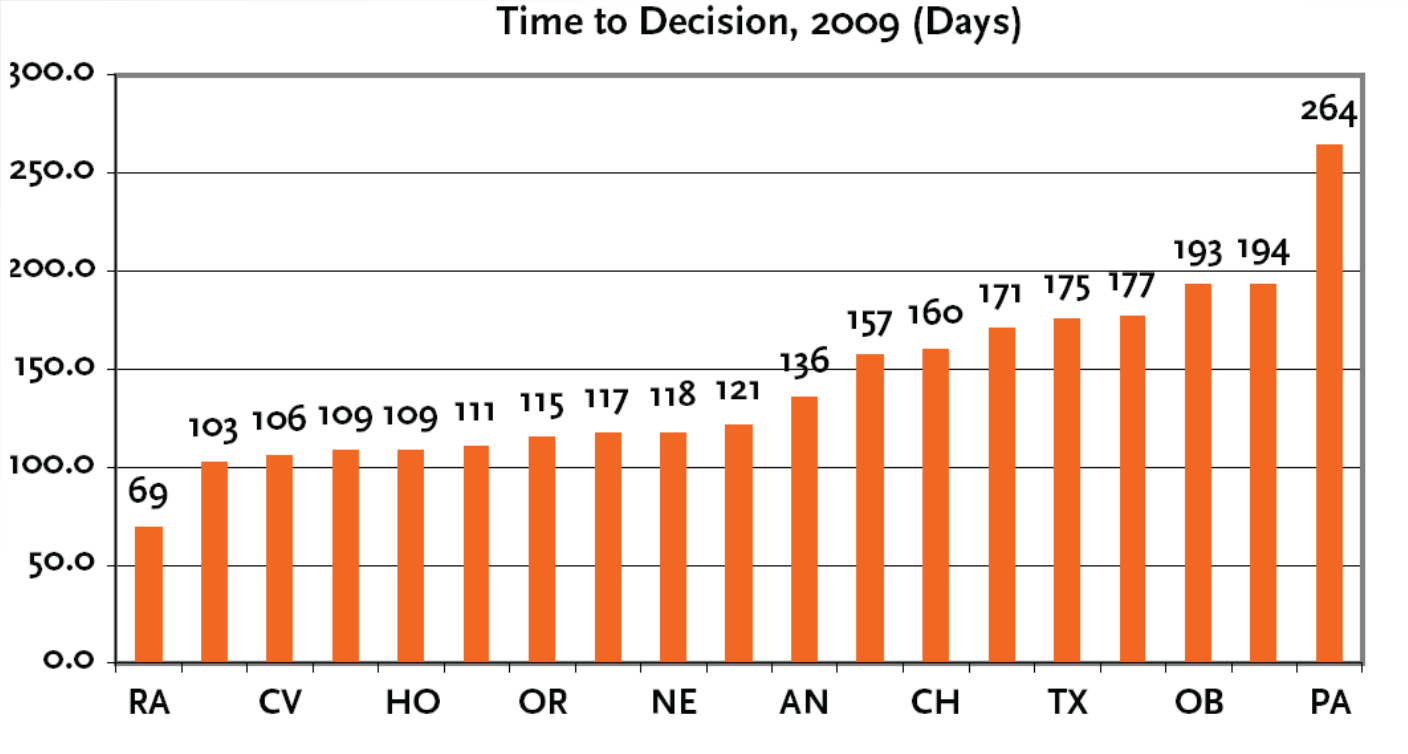
Massachusetts Medical Devices Journal, LLC, 2009. Eye on FDA 2009.

Class II Devices – The 510(k) Process



MassDevice. Eye on FDA 2009. Massachusetts Medical Devices Journal, LLC, 2009.

Average Review Time by Specialty



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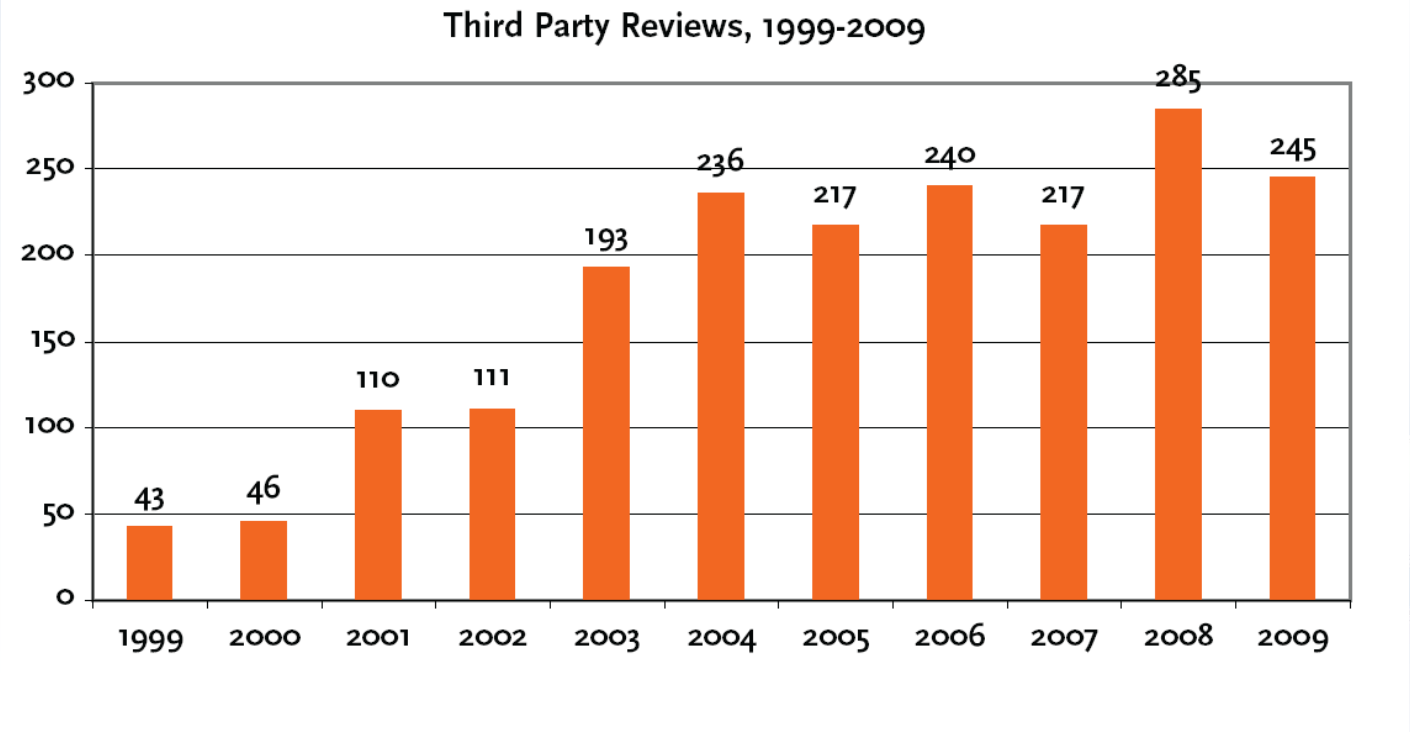
Third Party Reviews



Massachusetts Medical Devices Journal, LLC, 2009. Eye on FDA 2009.

The 510(k) Process – Current Environment

- Technological gap
  - How long can a device be substantially equivalent to a pre-1976 device?
- Generational change at FDA
  - ‘Baby Boomers’ retiring
  - Delays in recruitment and training of a new generation
    - Budget cuts
- Political pressures
  - Conservative agenda
    - Abortion (RU-486 12 year review)
  - Menaflex

Complaints and Challenges

- Complaints (sponsors) – review process lacks
  - Transparency
  - Predictability
  - Consistency
- Critics (public)
  - Not enough testing
  - Inappropriate clearances
- Challenges (FDA)
  - Ever-changing scientific landscape
  - New evidence of risks and benefits modify views of device / technology
  - Innovation vs. predictability and the role of change
  - Decisions affect:
    - US economy
    - US public health

2009 Review of 510(k) Program

- Parallel efforts (2009 – 2010)
  - External Review
    - Institute of Medicine (report expected summer 2011)
  - Internal Review
    - 510(k) Working Group
    - Task Force on the Utilization of Science in Regulatory Decision Making
- Town Hall Meetings
- Proposed recommendations
  - Immediate implementation
  - Proposed legal / regulatory revisions
  - Complete review following IOM report

New Initiatives

- Dual goals – protect and promote public health
- Interagency Council on Medical Device Innovation
  - Identify unmet needs
  - Facilitate development or redesign of devices to address unmet needs
- Memorandum of Understanding (MOU) with CMS
  - Streamline review process
    - Regulatory + reimbursement

Recommendations – I

- Based on 510(k) Working Group and Science Utilization Task Force
- Fostering medical device innovation
  - Streamline the premarket pathway for lower-risk novel devices (De Novo program)
  - Enhance science-based professional development for CDRH staff
  - Establish a network of external experts to better inform the review of cutting-edge technologies

Recommendations – II

- Enhancing regulatory predictability
  - Establishing a new “class IIb”
    - Clinical and/or manufacturing data
  - Predictability – “Notice to Industry” tool to communicate changes in expectations
  - Consistency – Clarify “substantial equivalence” review standard
  - Transparency – Establish Center Science Council as a new governance model
    - Head – Deputy Center Director for Science
    - Includes – experienced managers and employees
    - Responsible for overseeing science-based decision making process:
      - Premarket review
      - Audit and assessment of program performance
      - Resource for staff on scientific questions

Recommendations – III

- Improve patient safety
  - Require the up-front submission of more complete safety and effectiveness
    - Provide summary of ALL scientific information regarding safety and/or effectiveness of device
  - Create a searchable online, up-date, public, medical device db
    - Photographs and design schematics
    - Summaries of FDA review decisions
    - Up-to-date device labeling
  - Clarify CDRH's 510(k) rescission authority
    - Devices removed from market for safety concerns
    - Authority to rescind clearance and ban use as predicate

Future

- 510(k) process continues to evolve
- Globalization
  - Convergence of requirements across Globe
    - IIb
  - Harmonization Task Force