Changes in Regulatory Environment (US) and Implications for Early Stage Medical Device Companies

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Zvi Ladin, Ph.D.

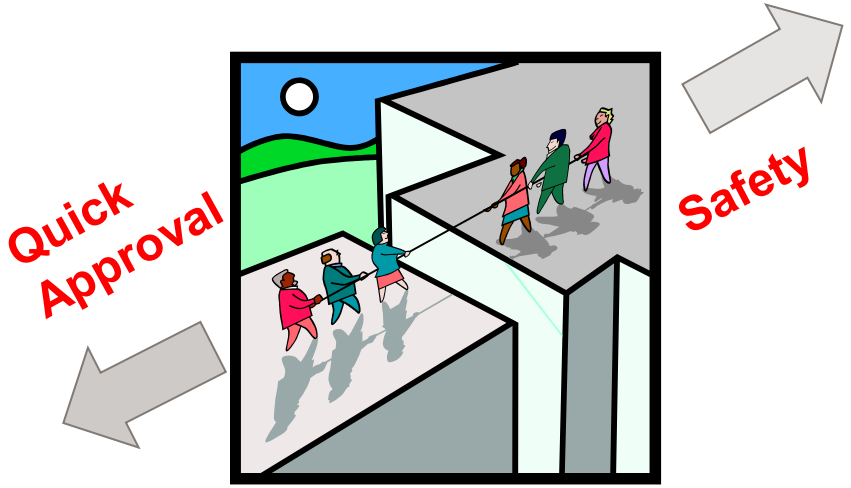
Overview

- Challenges of 510(k) program
- FDA reevaluation of 510(k) program
  - Task forces findings and recommendations
  - Institute of Medicine (IOM) review and recommendation
- Industry concerns(P T C C)
  - Predictability
  - Transparency
  - Consistency
  - Costs
- New CDRH initiatives
  - Review
  - Clinical trials
  - Homologation

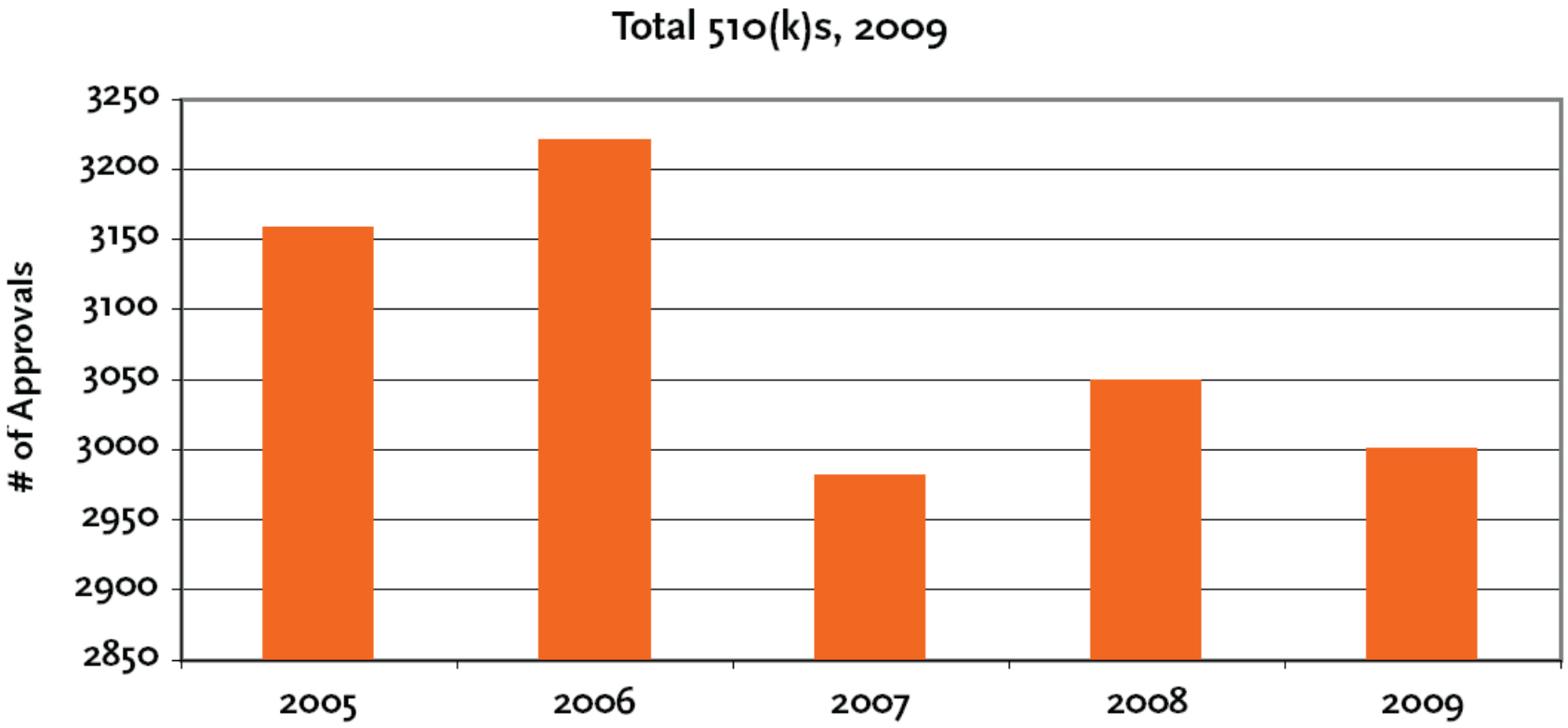
The Crystal Ball

The 510(k) Process – Environment (end 2000s)

- Technological gap
  - Substantially equivalence to pre-1976 device?
- Generational change at FDA
  - ‘Baby Boomers’ retiring
  - Delays in recruitment and training of a new generation
    - Budget cuts
- Political pressures (2000s)
  - Conservative agenda
    - Abortion (RU-486 12 year review)
  - Menaflex

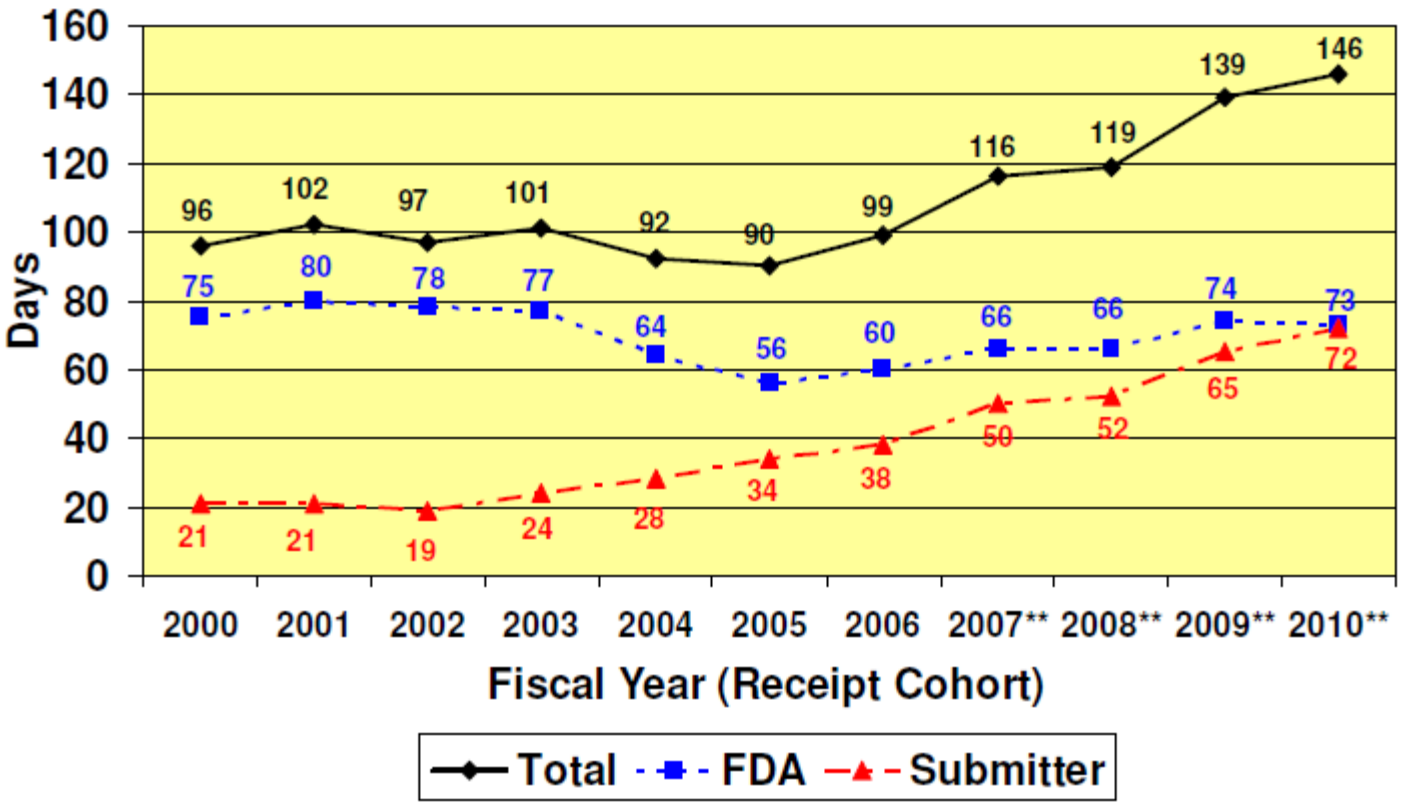


Cleared Medical Devices



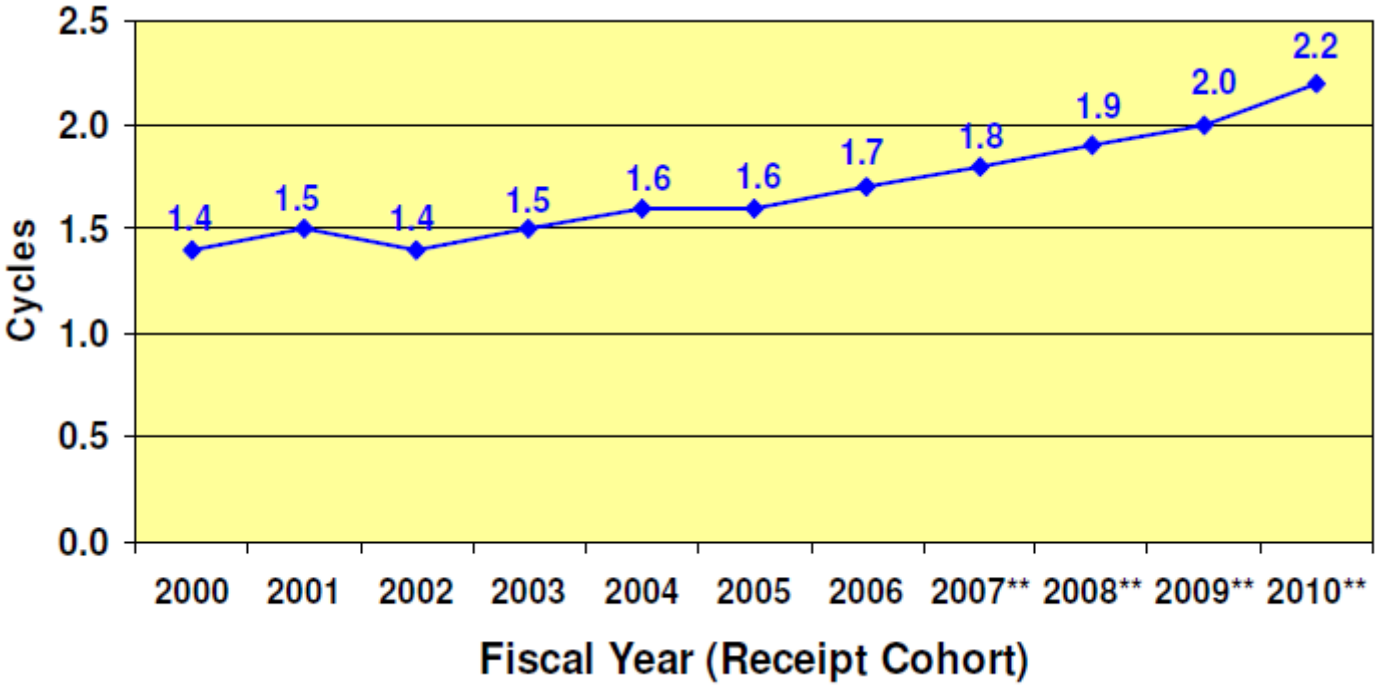
MassDevice. Eye on FDA 2009. Massachusetts Medical Devices Journal, LLC, 2009.

Average Time to 510(k) Decision *



*SE and NSE decisions only; times may not add to total due to rounding
**Cohorts still open as of September 30, 2011, data may change

Average Number of FDA Review Cycles *



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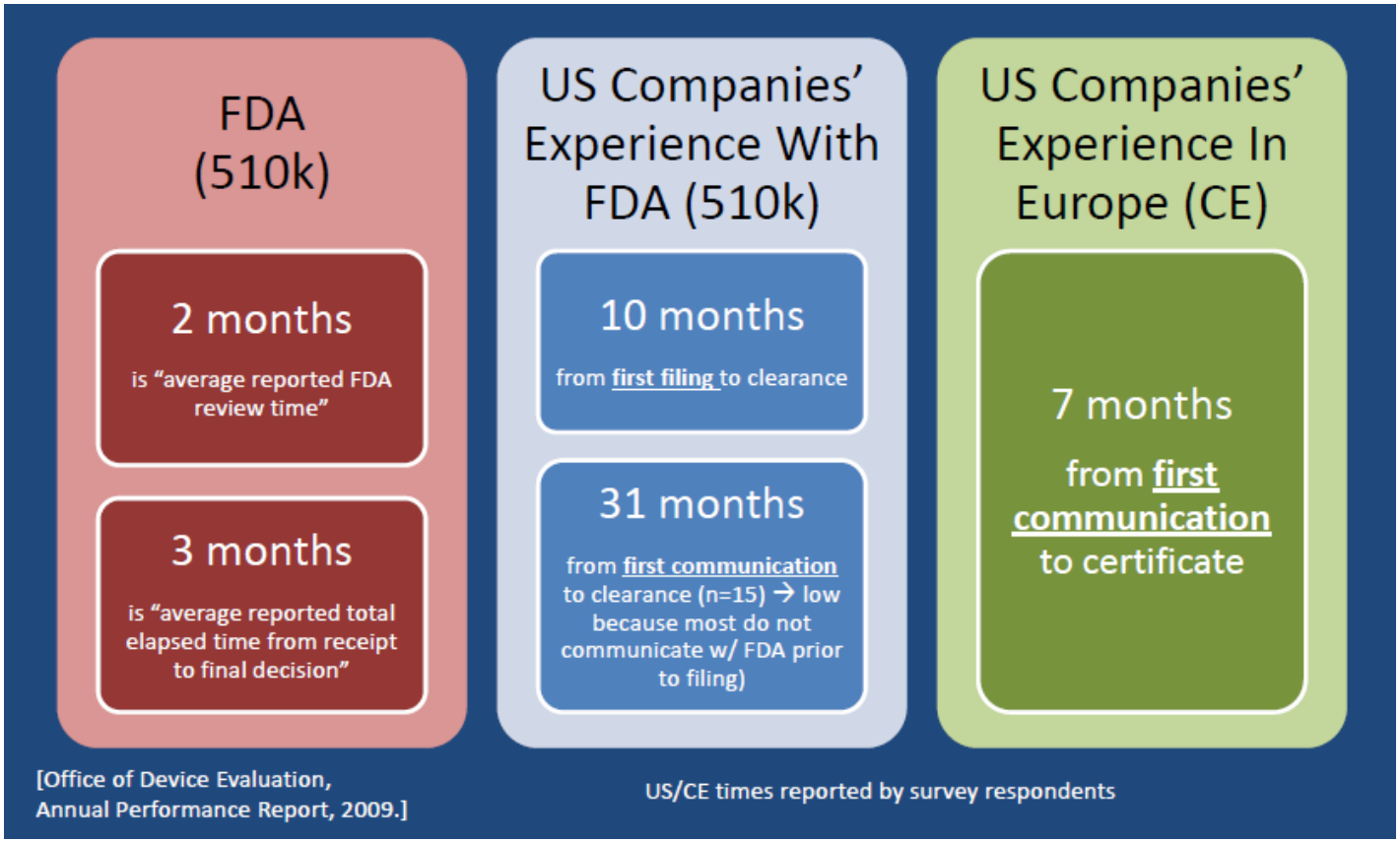
510(k) & CE timelines in US & Europe

Reported FDA transit times underestimate actual regulatory delay



Source: FDA Impact on U.S. Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies, November 2010

Cost of Concept to Clearance / Industry Perspective

- Average to clear 510(k) – $31 million*
  - $24 million on FDA-dependent/related

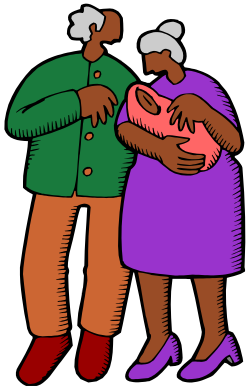
- Average to clear PMA – $94 million*
  - $75 million spent on FDA-dependent/related aspects

* Does not include reimbursement approval and sales/marketing costs.

Source: FDA Impact on U.S. Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies, November 2010

Me Too! 510(k) Process Problems

- 510(k) approval process loophole
  - The Domino effect
- Grandfathering pre-amendment devices



- Example:
  - Boston Scientific's ProteGen Sling, vaginal mesh implants (to treat urinary incontinence) used surgical mesh implanted in the abdomen (to treat hernias) as predicate
  - Johnson & Johnson subsequently received 510(k) clearance for Gynecare TVT (vaginal surgical mesh), based on its similarity to Boston Scientific's ProteGen Sling (1998)
  - J&J wasn't required to conduct clinical testing
  - ProteGen synthetic mesh was pulled from the market in 1999

Clearance of New Technologies

Public	Industry	FDA
Safety (MoM Prosthesis)	Predictability	Scientific / Technical
Limited Testing	Transparency	Innovation / Safety
Access to Innovation	Consistency	New Information (Risks) / Effect on Clearances
Costs	Costs	Costs

510(k) Review – Promote and Protect Public Health

Sept 2009
- Two internal groups: **510(k) working group** and **Taskforce on the utilization of science in regulatory decision making**
- **Institute of Medicine** (IOM) to independently review 510(k) process

Aug 2010
- Two preliminary reports released
- 55 recommendations

Oct 2010
- Public comment period ended for preliminary reports

Jan 2011
- 36 actions to improve the 510(k) program

July 2011
- IOM report released

Quality Issues with 510(k) Submissions

- Inadequate device description
- Discrepancies throughout submission
- Problems with Indications for Use
- Failure to follow or otherwise address current guidance document(s) or recognized standards
- Performance testing required for certain device types is completely missing
- Clinical data required for certain device types is completely missing

Source: http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/ucm263385.htm

New Initiatives

- Proposed recommendations
  - Immediate implementation
  - Proposed legal / regulatory revisions
  - Complete review following IOM report
- 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 – Innovation

- 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 – Regulatory Predictability

- Establishing a new “Class IIb”

- Predictability
  - Communicate expectations

- Transparency
  - Center Science Council

- Consistency
  - Clarify “substantial equivalence”

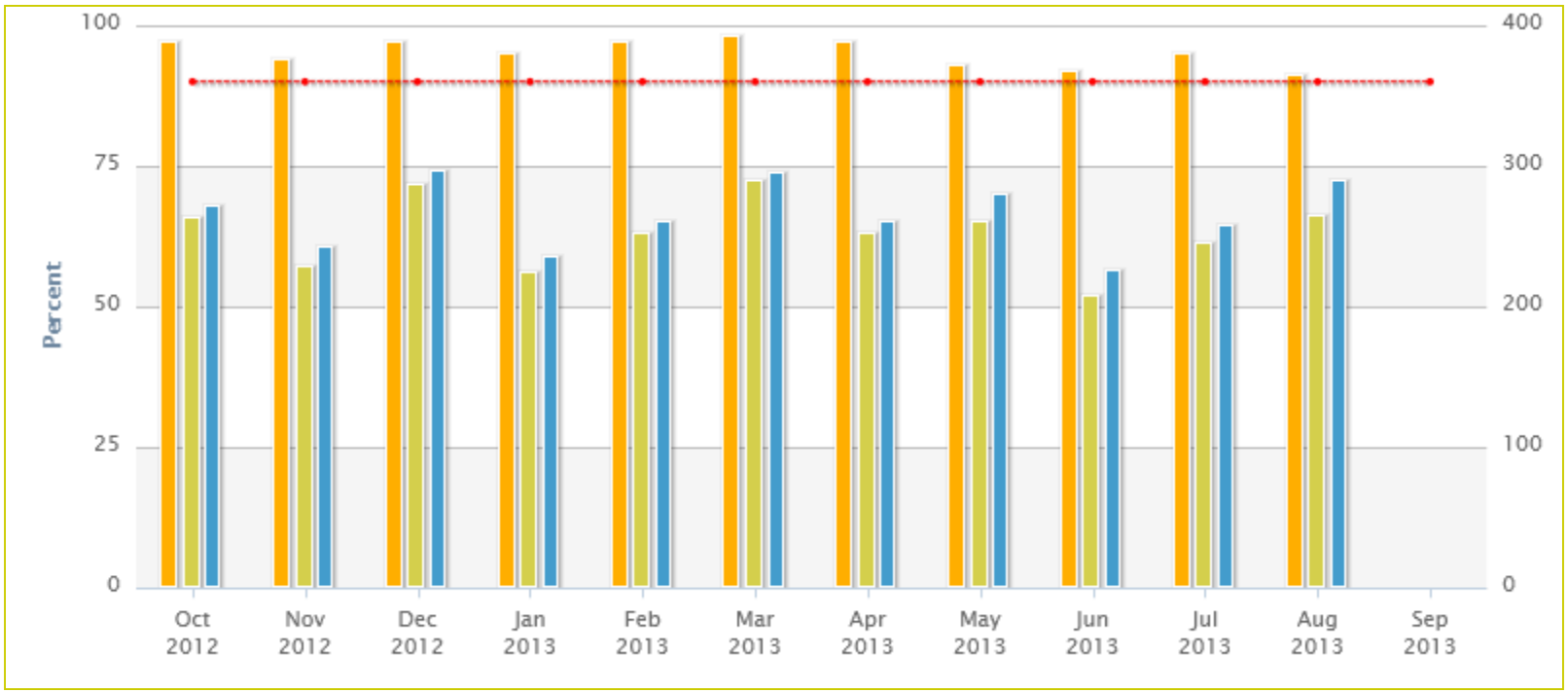
Recommendations – Improve Patient Safety

- More safety + effectiveness data
- Clarify CDRH's 510(k) rescission authority
  - Removal for safety concerns
  - Rescind clearance and ban use as predicate
- Searchable online, up-to-date, public device database
  - Photographs and design schematics
  - Summaries of FDA review decisions
  - Device labeling

CDRH Recommendations (Post 510(k) Review)

- Implement an "Assurance Case" Pilot Program
- Establish a Center Science Council
- Establish "Notice to Industry Letters" as a Standard Practice
- Clinical Trials Guidance
- Enhance Training
- Evaluation of Automatic Class III Designation (De Novo) Guidance
- Leverage External Experts
- 510(k) Paradigm Guidance
- Product Code Guidance
- Appeals Guidance
- Implement a Unique Device Identification (UDI) System
- Electronic Submissions

FDA Improved Performance – 2012/3



Percentage

Total number cleared within 90 days

Total number cleared

Innovation Pathway 2.0

Source: http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHInnovation/InnovationPathway/default.htm

Pilot Triage Program

- Create an incentive to submit good quality applications
- April 2, 2012 – October 2, 2012
- Quick Review Criteria
  - Pass quick review checklist
  - Pass a total product life cycle (Postmarket) search
  - Seek clearance for a device for which FDA has review experience and knowledge of expected performance
  - Not need for an extensive consult to complete 510(k) review
  - Contain a 510(k) Summary [and not a 510(k) Statement]
- Quick Review Tier – good quality submissions that fit quick review criteria; clear within 30 days
- Regular Review Tier - current normal 510(k) review process; clear within 90 days

Source: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm300308.htm

Facilitate US Clinical Trial

- Pre-Sub Meetings (December 2012)
  - Replaced ‘Pre-IDE’ process
  - Accommodates all submission types

- IDE Policy
  - Reject for safety only (June 2013)
  - First in human studies (September 2013)
  - Design of pivotal studies (November 2013)

Medical Device Development Tool

- New Guidance Document (November 13, 2013)
- Scientifically Validated Tool
  - Clinical outcome assessment (patient or clinician reported)
  - Test – detect or measure biomarker
  - Non-clinical assessment method or model
- CDRH Expectation
  - Within context of use – results can support regulatory decision
- Benefits
  - Broadly (industry + FDA) accepted
  - Faster decision-making

Special Reports, Workshops and Initiatives

- Patient Preference Initiative
  - Incorporating patient feedback into the regulatory process (September 2013)
- Personalized Medicine
  - *Paving the Way for Personalized Medicine* (October 2013)
- FDA / AGA (American Gastroenterological Association) Workshop
  - *Changing Regulatory and Reimbursement Paradigms for Medical Devices in the Treatment of Obesity and Metabolic Diseases* (December 2013)
- Medical Device Single Audit Program
  - Pilot program starting January 2014
  - Countries – Brazil, Canada, Australia (Japan – observer)

Next Steps

- Implementation of ongoing initiatives to improve the unpredictable, inefficient, and expensive regulatory processes
- Independent assessment of FDA device review process management
  - Phase 1: March 31, 2013 – September 30, 2014
  - Phase 2: October 1, 2014 – February 29, 2016
- Electronic submissions
  - January 28, 2015 – new standard for clinical trial data format
- International collaboration
  - Inspections
  - Clearances
- 510(k) – Closer to the end?

Thank You!

Contact information:

Boston MedTech Advisors, Inc.
990 Washington Street
Dedham, MA 02026
Ph. 781.407.0900
zladin@bmtadvisors.com