Medical Device Regulatory Innovation: An Engine for Transforming Medicine

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Food and Drug Administration
Center for Devices and Radiological Health
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Who We Are

CDRH is a team of 1,700 dedicated employees

- Physicians
- Engineers
- Biologists
- Chemists
- Physicists
- Statisticians
- Epidemiologists
- Toxicologists
- Nurses
- Veterinarians
- Pharmacologists
- Microbiologists
- Specialists in Public Health Education and Communication
- Lawyers
- Economists
Our Mission

• The mission of the Center for Devices and Radiological Health (CDRH) is to protect and promote the public health.
• We assure that patients and providers have timely and continued access to safe, effective, and high-quality medical devices and safe radiation-emitting products.
• We provide consumers, patients, their caregivers, and providers with understandable and accessible science-based information about the products we oversee.
• We facilitate medical device innovation by advancing regulatory science, providing industry with predictable, consistent, transparent, and efficient regulatory pathways, and assuring consumer confidence in devices marketed in the U.S.
# Medical Device Oversight

## A Risk-Based Approach

<table>
<thead>
<tr>
<th>CLASS</th>
<th>OVERSIGHT</th>
<th>EXAMPLE</th>
</tr>
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<tbody>
<tr>
<td><strong>Class I</strong></td>
<td>FDA does not review any premarket information, with the exception of a small subset of Class I “reserved” devices</td>
<td>Bandages</td>
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<tr>
<td>or low-risk devices</td>
<td></td>
<td></td>
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<tr>
<td>(about 50% of all medical devices)</td>
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<td></td>
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<tr>
<td><strong>Class II</strong></td>
<td>FDA generally reviews 510(k) submissions for these devices. Require a demonstration of substantial equivalence to a legally marketed device</td>
<td>Glucose test strips and infusion pumps</td>
</tr>
<tr>
<td>or moderate-risk devices</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Class III</strong></td>
<td>FDA generally reviews PMAs containing clinical and non-clinical data to determine whether there is a reasonable assurance of safety and effectiveness for these devices</td>
<td>Heart valve replacements and diagnostic tests used to select ovarian cancer patients for a drug regimen</td>
</tr>
<tr>
<td>or high-risk devices</td>
<td></td>
<td></td>
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<tr>
<td>(about 40 PMAs a year)</td>
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Common “Pitfalls”

• **Poor Submission Quality**
  - Product description insufficient
  - Inconsistencies throughout the document
  - Supportive data insufficient or missing without rationale
  - Prior interactions/discussions not addressed
  - Hard to find relevant information

• **Inadequate Responses to Data Requests**

• **Poor Communication**
Advice for Sponsors

• Talk to us early and often

• Know what you need to know and what you don’t know
  ▪ Don’t assume
  ▪ Get professional (regulatory) help if you need it

• Plan ahead
  ▪ Consider what you need to do for FDA approval and payer coverage

• Stay abreast of new regulatory and scientific developments

• The most important thing you can do is good science
We face a critical public health challenge

The U.S. regulatory standard for market approval protects patients by setting a high public health bar but imposes costs that make the U.S. marketplace less attractive for innovators thereby delaying patient access to important technologies

The solution is to reduce the time and cost of the total product life cycle...

device development, assessment, review, manufacturing, monitoring, and reimbursement – without compromising the reasonable assurance of safety and effectiveness standard
New Innovations

New Technologies Create New Regulatory Challenges

• Wearable, implantable, portable devices
• Miniaturized devices
• Combination products
• Tissue re-engineering
• Moving from minimally invasive to least-invasive approach
• Robotics
• Smart and interoperable devices
• Information technology
• New age imaging
• Next generation “omic” sequencing
2014 - 2015 Strategic Priorities

2016 - 2017 STRATEGIC PRIORITIES WILL BUILD ON OUR CURRENT ACCOMPLISHMENTS
2014 - 2015 CDRH Strategic Priorities

- Strengthen the Clinical Trial Enterprise
- Strike the Right Balance Between Premarket and Postmarket Data Collection
- Provide Excellent Customer Service
## Regulatory Innovation Can Drive Technological Innovation

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Flexible Regulatory Paradigms
Continuum of Clinical Study Onset and Market Entry Points

CDRH Vision

Benefit-Risk Tradeoffs

Clinical Trials
Early Feasibility Study Paradigm Guidance (2013)

Premarket-Postmarket Balance
Expedited Access Pathway Program (2015)
Balancing Premarket and Postmarket Data Collection (2015)

Science of Patient Input
Medical Device Innovation Consortium (MDIC) Patient Centered Benefit-Risk Project
2014 - 2015 CDRH Strategic Priorities
Strengthen the Clinical Trial Enterprise

Benefit-Risk Determinations
IDE Decisions Guidance
Early Feasibility First in Human Policies
Implemented FDASIA

Clinical Trials Program
2014 - 2015 CDRH Strategic Priorities
Strengthen the Clinical Trial Enterprise

CDRH FY 2015 Target: By June 30, 2015, reduce the overall median time to full appropriate IDE approval to 30 days.

![Bar chart showing median days to IDE study full approval from FY 2011 to FY 2015]

- FY 2011: 442 days
- FY 2013: 215 days
- FY 2014: 101 days
- FY 2015: 30 days

Source: Center for Devices and Radiological Health
2014 - 2015 CDRH Strategic Priorities
Strengthen the Clinical Trial Enterprise

CDRH FY 2015 Target: By June 30, 2015, increase the number of early feasibility/first-in-human IDE studies submitted to each premarket Division compared to FY 2013 performance.

The number of early feasibility studies submitted increased in 6 of the 7 ODE review divisions

50% During the first 9 months there was a 50% increase EFS submissions in CDRH as a whole (compared to FY13)

In addition CDRH:
✓ Draft guidance on IDE Benefit-Risk
✓ Draft guidance on Adaptive Design for Medical Device Clinical Studies
2014 - 2015 CDRH Strategic Priorities
Strengthen the Clinical Trial Enterprise

• Next Areas of Focus include:
  ▪ Quality by Design for medical device clinical studies
  ▪ Improved IDE submission quality
  ▪ Continued growth of EFS Program
  ▪ Leveraging evidence from clinical experience
  ▪ Clinical trial simplification
  ▪ Use of modeling to reduce clinical trial size*

*Advancing medical device regulatory science generally, such as through the Medical Device Innovation Consortium (MDIC), is critical
Medical Device Innovation Consortium

A Public-Private Partnership collaborating on Regulatory Science to make patient access to new medical device technologies faster, safer, and more cost-effective
What is Regulatory Science?

The science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of FDA-regulated products

- Benefits patients by speeding the rate of important technologies reaching market
- Reduces time and resources needed for device development, assessment, and review. For example:
  - Can lead to quicker, more efficient device approvals
  - Can decrease the size and duration of pre-market clinical trials

Faster, Safer, More Cost-effective

FDA Strategic Plan, August 2011
Advancing Regulatory Science at FDA
2014 - 2015 CDRH Strategic Priorities
Strike the Right Balance Between Premarket and Postmarket Data Collection


CDRH FY 2015 Target: By June 30, 2015, review 75 percent of device types subject to a PMA that have been on the market to determine whether or not to shift some premarket data requirements to the postmarket setting or to pursue down classification, and communicate those decisions to the public.

85% CDRH reviewed 85 percent of device types subject to a PMA that have been on the market.

In addition CDRH:
✓ Solicited comments on the 69% of devices types reviewed by December 2014
✓ Effectively downclassified over 120 devices from Class II to Class I
✓ Issued final guidance document on achieving the right balance between premarket and postmarket data collection
✓ Launched the Expedited Access Pathway Program
2014 - 2015 CDRH Strategic Priorities
Strike the Right Balance Between Premarket and Postmarket Data Collection

Expedited Access Pathway  Launched the Expedited Access Pathway Program in April 2015 for breakthrough devices

• Eligible devices are those subject to a PMA or de novo intended to treat or diagnose a life-threatening or irreversibly debilitating disease and address an unmet need
• Early, ongoing, and extensive interaction with review team, engagement by senior management, assignment of a case manager, and collaborative creation of a Data Development Plan
• Where appropriate, some premarket data collection shifted to the postmarket setting for PMA devices
2014 - 2015 CDRH Strategic Priorities
Provide Excellent Customer Service

CDRH FY 2015 Target: By June 30, 2015, achieve at least 80 percent customer satisfaction.

OVERALL CUSTOMER SATISFACTION RATING
As of June 30, 2015

88%

EXTERNAL CUSTOMER RATING
91%

INTERNAL (FDA) CUSTOMER RATING
84%
Partnering with Patients

Investing in the Science of Patient Input

• Patient Preference Initiative
  • May 2015 Draft Guidance
  • May 2015 MDIC Framework
• Expanded use of Patient Reported Outcomes

Establishment of a Patient Engagement Advisory Committee
However, the most important means to successful market entry, adoption, and safe use is knowledge through evidence generation and experience.
Key Challenges for Knowledge Generation in the Medical Device Ecosystem

• Significant Inefficiencies in Our Healthcare System: We do not make good use of data and knowledge generated every day as a part of routine healthcare
  ▪ Inadequate interoperability
  ▪ Inadequate data quality and completeness
  ▪ Inadequate methodologies
  ▪ Different definitions

• Data Silos
  ▪ Competition over data rather than only over what we do with the data, such as making better technologies
Key Challenges for the Medical Device Ecosystem

• Regulatory paradigms are out of step with rapid technology innovation cycles and data generation

• Rapid technological innovations without adequate knowledge about their impact on people

• Reimbursement models that do not encourage knowledge generation and smart innovation

Overall, the whole system costs too much and change won’t come easy
Where Have We Been?
Digital Revolution and the Information Age

- **Digital Revolution** begins
  - transistor invented in 1947, leading the way to computers
  - first message sent over the ARPANET in 1969

1970s
- First public digital HDTV broadcast – 1990 World Cup
- **Information ‘Superhighway’**
  - internet expanded quickly, every country had connection
  - 65% of households owned a computer

1980s
- 15% of U.S. households owned a computer and 30% with children under 18 owned one
- First digital camera
- **World Wide Web** invented

1990s
- Cell phones, text messaging, over 1 billion internet users, and **HDTV became standard** in television broadcasting

2000s
- Widespread use and interconnectedness of mobile networked devices and mobile telephones, internet websites and resources
- Social networking becomes the de facto standard in digital communication
- **Cloud computing** enters mainstream
- As of May 2014, there were nearly **7 billion mobile** subscriptions worldwide

Origins
- Home computer, time-sharing computers, video game consoles and age of arcade video
The Accelerating Pace of Change

1. The accelerating pace of change...
   - Agricultural Revolution: 8,000 years
   - Industrial Revolution: 120 years
   - Light-bulb: 99 years
   - Moon landing: 22 years
   - World Wide Web: 9 years
   - Human genome sequenced

2. ...and exponential growth in computing power...
   Computer technology, shown here climbing dramatically by powers of 10, is now processing more each hour than it did in its entire first 90 years

3. ...will lead to the Singularity
   - Apple II: At a price of $1,298, the compact machine was one of the first massively popular personal computers
   - UNIVAC I: The first commercially marketed computer, used to tabulate the U.S. Census, occupied 943 cu. ft.
   - Colossus: The electronic computer, with 1,500 vacuum tubes, helped the British crack German codes during WW II

http://content.time.com/time/interactive/0,31813,2048601,00.html
It has been estimated that as much as 90% of all data in the world has been generated in the past two years.
## Digital Revolution and the Information Age

### Benefits and Costs

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<td>• Access to more information and people</td>
<td>• Quality of information</td>
</tr>
<tr>
<td>• Faster creation of new information</td>
<td>• Too many silos as information became a commodity</td>
</tr>
<tr>
<td>• Longitudinal connection of data</td>
<td>• Content and structure of databases, as well as difficulties and costs of creating and maintaining comprehensive databases</td>
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Where Could (Should) We Go?
Learning Medical Device Ecosystem: A Neural Network

Flexible regulatory paradigms combined with knowledge commons and a national evaluation system (plus supportive reimbursement models) can lead to a paradigm shift for the medical device ecosystem.

This approach can incentivize the development and use of important new devices and other technologies that improve the health and the quality of life of patients while increasing the return on investment of our healthcare dollars.
Flexible Regulatory Paradigms fit the needs of specific types of devices for knowledge generation, technological innovation and timely patient access by applying rational benefit-risk tradeoffs

Knowledge Commons allow for sharing data and crowdsourcing knowledge

A National Evaluation System strategically gathers, generates, aggregates, and analyzes evidence from clinical experience under ecosystem rules and governance
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Should we have a progressive/conditional approval pathway?
Flexible Regulatory Paradigms

Data Generation: There’s More than One Way to Skin a Cat

- Bayesian Statistics Guidance (2010)
- Evidence from Clinical Experience (“Real World” Observational) Data Draft Guidance under development
  - Critical to address “noise” and biases, such as by imbedding randomization into the system
- Medical Device Innovation Consortium (MDIC) Computer Modeling Project
- Use of Modeling in Clinical Trials Paper under development

But, regardless of the approach, the data must be sufficiently robust
Flexible Regulatory Paradigms

Smart Regulation When You Need It
No Regulation When You Don’t

Extensive deregulation of low-risk digital health technologies

- Mobile Medical Apps Guidance (2013)
- Medical Device Data Systems Guidance (2015)
- General Wellness Claims Draft Guidance (2015)

New framework for Software as a Medical Device under development intended to meet the needs of rapid innovation cycles, such as through greater reliance on quality system controls rather than premarket review
Knowledge Commons

Knowledge Commons make curated information available to a community to do research, and generate and apply new knowledge.

2014 FDA White Paper outlines possible approach to advance these technologies that would greatly reduce time and cost by leveraging data in high-quality, curated genetic databases as an alternative to conducting new clinical trials, thereby letting the clinical community *crowdsource data* to demonstrate clinical validity based on *levels of evidence* and *expert review*. 

Adapting regulatory framework to address new technologies: Next Generation Sequencing (NGS)
FDA’s Vision for a National System
For the Ecosystem, Governed by the Ecosystem

• Develops and communicates an evolving understanding of device benefits and risks throughout their marketed life using high-quality, linked electronic health information
• Identifies potential safety signals in near real-time from a variety of privacy-protected data sources serving as a safety net
• Reduces burdens and costs of medical device postmarket surveillance
• Facilitates clearance and approval of new devices or new uses of existing devices
Proof of Concept
Use of Real World Evidence to Expand Minimally Invasive Heart Valve Replacement Indications

Society of Thoracic Surgeons (STS) and American College of Cardiology (ACC) Transcatheter Valve Therapy (TVT) Registry

• Used for regulatory decision making: expansion of use, label change

• Linked to claims data for longitudinal study of transcatheter aortic valve replacement

• Increased speed and efficiency of studies
In February 2015, the multi-stakeholder Planning Board, convened by the Brookings Institution, issued a report with recommendations for how to establish the national system:

- Provides a pathway to realizing a national system that harnesses novel data sources, modern analytical techniques and the participation of all stakeholders to optimize patient care.
- Set out an organizational structure and directions for pilots.
- Proposed next steps:
  - 5-year Implementation Plan
  - Pilots

National “Surveillance” System

Current Step: Medical Device Registry Task Force Report

- Builds on the core strategy of the White Papers and the Planning Board Report
- Discusses the role of registries in the evolving National Medical Device Evaluation System
- Provides a direction for the future of registries

National Evaluation System

Core Strategy

• Build on existing information systems
• Link registries to longitudinal data (claims data, Sentinel, PCORnet, EHRs)
• Establish “Coordinated Registry Networks”
• Remain flexible to accommodate evolution of parts (IT, medical device development, science, health care delivery system)
Regulating Innovation with Uncertain Quality: Information, Risk, and Access in Medical Devices

According to the authors, “For the set of devices on which we have data, we estimate that the US is close to the optimal policy”

**Finding:** FDA required clinical studies drive device use but also delay patient access and increase market access costs

**Conclusion:** “Some FDA reform proposals advocate for more relaxed premarket requirements but enhanced postmarket surveillance. The logic behind this proposal is straightforward.... We...find that if post-approval learning rates approach those we observe from clinical trials at a comparable cost, the benefits from such a policy change are substantial.”
Learning Medical Device Ecosystem

INFORMATION FLOW

TIME TO MARKET

Premarket Review

- Expedited Access Pathway
- Benefit Risk

Premarket Decision

Postmarket Surveillance System

- Evidence from Clinical Experience
- “Safety Net”
Thank You