Healthcare 2.0
From ACOs to Telemedicine and Beyond

December 16, 2015

BOSTON | GERMANY | ISRAEL

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New Thinking at the FDA – Back to Basics

The Key – **Risks** (and Benefits)

December 2015

Zvi Ladin, Ph.D.
Principal
Boston MedTech Advisors
Boston MedTech Advisors

Celebrating 11 Years

170+ companies
### Engagements

*(partial list)*

<table>
<thead>
<tr>
<th>Aesthetic Medicine</th>
<th>Ambulatory monitoring</th>
<th>Anesthesiology</th>
<th>Brain / Neurosurgery</th>
<th>Cancer Therapies</th>
<th>Cardiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical Care</td>
<td>Cryosurgery</td>
<td>Dermatology</td>
<td>Durable Medical Equipment</td>
<td>Emergency Medicine</td>
<td>General Surgery</td>
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<td>Health IT</td>
<td>Hepatology</td>
<td>Home care</td>
<td>Interventional Cardiology</td>
<td>In-Vitro Diagnosis</td>
<td>Interventional Radiology</td>
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<td>Neurology</td>
<td>Orthopedic</td>
<td>Patient Monitoring</td>
<td>Pulmonary</td>
<td>Radiology / Imaging</td>
<td>Rehabilitation Medicine</td>
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<tr>
<td>Robotics</td>
<td>Sleep Medicine</td>
<td>Spine Surgery</td>
<td>Telemedicine</td>
<td>Vascular Medicine</td>
<td>Wellness / mHealth</td>
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Engagements (sample)*

- Start-ups through Fortune 500 companies
  - Diagnostic, therapeutic and monitoring technologies
  - Healthcare providers - medical practices, clinics and hospitals
  - Consumer medical products and services
- Technology incubators, technology transfer and licensing offices
- Investors (private, institutional)
- Expert Witness (International, State, Federal)

* Including advisors’ prior relationships
170+ companies
2015 ‘Hot Topics’ at FDA – Broad Strokes

- Balancing Device Risks and Benefits
  - Exemption of Certain Class II/I from Notification Requirement
  - Expediting Access – Addressing Unmet Needs
    - Life threatening or
    - Irreversibly debilitating disease or condition
  - Early Detection System for Device Problems/Failures – NMDES
    - Permanent Clinical Trials

- Harmonizing Safety, Effectiveness and … Reimbursement

- Digital Health Revolution
  - Mobile Medical Apps
CDRH Vision – Interconnectivity / Total Product Life Cycle

- Vision
  - Continuum – from pre- to post-market

- Reality
  - Pre-market development
  - Regulatory assessment
  - Regulatory clearance
  - Post-market evaluation

Sometimes...
Market Failures of Cleared Medical Devices

2009

Medtronic pacemaker recall announced

WASHINGTON, June 17 (UPI) -- The U.S. Food and Drug Administration announced the recall of some Medtronic Inc. Kappa and Sigma pacemakers that might cause serious problems or death.

Recall of Defective Glucose Test Strips

WebMD

Recall of Defective Glucose Test Strips

Dec. 22, 2010 - The FDA says it is working with Abbott Diabetes Care to recall 3.59 million defective glucose test strips -- sold under a variety of brand names -- that may make blood glucose levels look low than they really are.

December 16, 2011

Heart Device Parts Recalled

St. Jude Medical said on Thursday that its Riaza defibrillator leads, which the company stopped selling last year, had been recalled by the Food and Drug Administration because of their potential to injure or kill patients.

Transvaginal Mesh Recall

May 17, 2013

The New York Times

J. & J. Unit Phasing Out All-Metal Hip Devices

The orthopedic unit of Johnson & Johnson said Thursday that it was phasing out production of all-metal replacement hips, a move reflecting an industrywide trend to abandon the once widely used implants because of high early failure rates.

BOSTON MEDTECH ADVISORS
More Experience ► Better Results
Goals – Combine Clinical Research and Patient Care

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<th>Clinical Research</th>
<th>Clinical Patient Care</th>
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<tbody>
<tr>
<td>• <strong>Limited</strong> size</td>
<td>• <strong>Large</strong> number of patients</td>
</tr>
<tr>
<td>• <strong>Select</strong> sites</td>
<td>• <strong>Various</strong> care venues</td>
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<tr>
<td>• <strong>Reductionist</strong> inclusion/exclusion</td>
<td>• <strong>Expansionist</strong> inclusion/exclusion</td>
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<tr>
<td>• <strong>Detailed</strong> information gathered</td>
<td>• <strong>Limited</strong> information gathered</td>
</tr>
<tr>
<td>• <strong>Limited</strong> generalizability</td>
<td>• <strong>Generalizable</strong></td>
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**Clinical Research** - Focuses on limited data collection and analysis in specific, research-oriented settings.

**Clinical Patient Care** - Emphasizes broad, generalizable outcomes from diverse patient populations.
Development of National Medical Device Evaluation System (NMDES)

- **2012** – FDA Initiative to strengthen Device Post-market Surveillance
- **2014** – two parallel groups (MDEpiNet + MDRTF)
  - **MDEpiNet** Medical Device Epidemiology Network
  - **MDRTF** – Medical Device Registries Task Force
  - Support better regulatory decisions
  - Serve stakeholders – medical device innovation ecosystem
  - Planning Board created, funded
    - Patient safety
    - Post-market represents all stakeholders
      - Patients / Regulators / Manufacturers / Payers

- **2015** – Board Recommendations
  - Public-Private Partnership (PPP) ([http://mdepinet.org](http://mdepinet.org))
  - Address needs of all stakeholders
  - **Eliminate discontinuities** in device evaluation and surveillance existing within total product life cycle
  - Develop and maintain:
    - Methodologic approaches
    - National and international scientific infrastructure
  - Promote collaborative, pre-competitive focus on novel, efficient, informative approaches to:
    - Device benefit/risk and safety surveillance challenges
    - Think-tank programs, publications, disease specific/device specific working groups, research projects
Long-Term Device Performance Studying

- National Medical Evaluation System (FDA)
  - Source: Report – August 20, 2015
  - Medical Device Registry Task Force & Medical Devices Epidemiology Network

- Recommendations
  - Multi-pronged approach – support different stakeholders
  - Electronic Health Records (EHR) – key for implementation
  - Unique Device Identifier (UDI) in electronic health data
  - Minimize burden of data capture
  - Protection of patients/privacy
  - Building on existing capabilities

Plan:
- Years 1 – 2: Incubator project to develop 5-year plan
- Years 3 – 7: Implementation
New Paradigm for PMS* – National Device Evaluation System

- Coordinated Registry Networks (CRN)
- Four Stakeholders
- Different
  - Interests
  - Information
  - Goals
  - Uses
- ‘Same’ information

* PMS – Post-Marketing Surveillance
NMDES – Sources of Information

- National Medical Device Evaluation System
  - Multiple sources of information available
    - **EHR** – Electronic Health Record
    - **UDI** – Unique Device Identifier
    - PMS (Post-Marketing Surveillance) Registries
    - Claims data (payers/administrative)
Examples of Existing Registries

- **TVT**
  - Transcatheter Valve Therapies
  - Registry linked to administrative claims data
  - Connects
    - device- and procedure-data
    - Long-term follow-up

- **ICOR**
  - International Consortium of Orthopedic Registries
  - Global distributed network
  - Early detection
    - Safety signals

Common challenges:
- Interoperability
- Standardization
Principles for Establishing CRN Functionality

- Device identification
- Use of standardized
  - Clinical vocabulary
  - Common data elements
  - Outcome definitions
- Generalizable interoperability solutions
  - Linking disparate data sources
- Creating partnered, inclusive governance
- Develop value-based incentivized sustainability

- Target – Incubator Project
  - Serious consequences of device failures
  - Expected rapid uptake
  - Long-term safety and effectiveness not understood
  - Design variations
  - Variable performance
  - Procedure – Operator dependent
  - Higher costs
  - Best practice – unknown
  - Problems with similar devices
  - Challenges in collecting outcome
FDA / CMS Memorandum of Understanding

• Effective Date – June 2015
• Federal Partners
• Covers all regulated products
• Goals
  • Promote collaboration
  • Enhance
    • Knowledge
    • Efficiency
  • Information sharing

• Substance
  • Point of contact
    • Director, Coverage and Analysis Group, CMS
    • Associate Commissioner of Policy and Planning, FDA
  • Current mode – response to requests for information
  • Reasonable timeline
  • Protection against unauthorized disclosure
Digital Health Revolution

• ~500M smartphone users worldwide use health-related apps

• 58% of smartphone users have ≥ 1 health-related app

• By 2017 – app market projected to reach $26B
FDA Mobile Medical App Guidance

• **Mobile app**
  - Software that can be run on a mobile platform, or
  - Web-based software application tailored to mobile platform but executed on server

• **Regulated mobile medical app if it fits within the definition of medical device:**
  - Intended for use in the diagnosis of disease or other conditions;
  - Intended for use in the cure, mitigation, treatment, or prevention of disease; or
  - Intended to affect the structure or any function of the body.

• MMA’s in 2013:
  - >13,000 health and fitness apps for consumers
  - >5,000 apps for medical professionals

• Only 103 were FDA-regulated

• Currently there are >100,000 mobile health apps available
Digital Health Revolution

- FDA – mobile technologies … “opening new and innovative ways to improve health and health care delivery.”
  - Only minority of apps that pose a higher risk would be regulated
- Most FDA-regulated apps – either stand-alone or accessories to existing medical devices
  - Smartphone function – ‘user interface’
  - MMAs future – smartphone/tablet hardware and software to perform more advanced functions

- FDA established 2015 guidelines for:
  - General Wellness (1/20/2015): Policy for Low Risk Devices
  - Mobile Medical Apps (MMA) (2/9/2015):
    - FDA’s focus – higher risk technology products
    - New guidance – implemented more closely calibrated risk-based approach.
2015 MMA Guidance Defined Three Categories

- **Unregulated**: Low-risk apps for promoting “general health or wellness” – unlikely to be regulated
  - e.g., exercise trackers and heart-rate monitors used in fitness regimens

- **Enforcement Discretion**: includes disease-focused apps that work as simple professional calculators or that provide coaching for patients
  - e.g., measuring and calculating mean arterial pressure, or assessing a Glasgow Coma Scale score

- **Regulated**: MMA’s “whose functionality could pose a risk to a patient’s safety if the mobile app were to not function as intended”
  - Apps that connect to medical devices in order to control the device, or for active patient monitoring or medical data analysis
    - Considered as an ‘accessory’ and regulated as the connected device (e.g., software that controls delivery of insulin by transmitting control signals to a pump)
  - Apps that transform the mobile platform into a regulated device
    - Regulated as the device into which it has been transformed (e.g., an app that allows for the attachment of a transducer to convert a smartphone into a stethoscope)
  - Apps that perform patient-specific analysis, diagnosis or treatment recommendations
    - e.g., an app that uses patient-specific information to calculate dosage or create a dosage plan for radiation therapy
MMA Concerns and Requirements

Safety Issues:

- **Connectivity** — MMA’s may be subject to unintentional interference or service interruptions
- **Data integrity** — Electromagnetic interference or single-event upsets may result in the corruption of data being received or transmitted by MMA
- **Cyber security** — Potentially vulnerability to cyber-attack, either through malware, virus-corrupted messages or other malicious activities
- **Updating protocols and procedures** — MMA’s, like other software products, are subject to periodic updates to address coding errors or to provide security patches
- **Display size and resolution** — Mobile platforms offer displays in a variety of sizes and resolutions and may unintentionally distort information displayed

Regulatory Requirements:

- Establishment registration and medical device listing
- Premarket submission for approval consistent with the risk classification
- Quality system regulation
- Product labeling
- Adverse event reporting
- Device specific regulations (e.g., wireless medical devices or home use)
MMA Classifications

- **Class II device (regulated based on IFU)**
  - e.g., SmartTouch by Nexus6 (K133951; 04/25/2014) is a smartphone-connected inhaler intended as an electronic data capture accessory for recording actuations of prescribed Metered Dose Inhaler (MDI) usage with a handful of indications: in clinical trials; in clinical practice, and for patient self-management.
    - Regulation number: 868.5630: Nebulizer; product code CAF

- **Unclassified**
  - e.g., DANA by Anthronix (K141865; 10/15/2014) is a mobile application for neurobehavioral assessment both in-clinic and out-of-clinic settings. It is indicated to provide clinicians with objective measurements of reaction time (speed and accuracy) and standardized health assessments to aid in the assessment of an individual’s medical or psychological state.
    - Unclassified; Product code LQD: Recorder, Attention Task Performance

- **Premarket Approval (PMA)**
  - e.g., Frontier by St. Jude Medical (P030035/S098; 04/10/2014) which enables a mobile platform to function as a user interface for their Merlin PCS programmer, thereby updating the previously approved PMA device.
    - Product code NIK: Defibrillator, Automatic Implantable Cardioverter, with Cardiac Resynchronization (Crt-D)
MMA Classifications

- **Investigational Device Exemption (IDE)**
  - e.g., Freedom Spinal Cord Stimulator (SCS) System by Stimwave (K150517; 6/5/2015) is an iPad Programmer for Spinal Cord Stimulation. IDE to launch an 80-patient clinical trial utilizing the wireless miniature eight electrode, multi-programmable neurostimulator device for the relief of chronic back and leg pain. The iPad is used in the clinical setting to give advanced programming options to the Wearable Antenna devices.
    - Regulation Number: 882.5880: Stimulator, Spinal-Cord, Implanted (Pain Relief); Product Code: GZB

- **De Novo**
  - e.g., Dexcom Share Direct Secondary Displays by Dexcom, Inc. (DEN140038; 01/23/2015) is a software device (smartphone apps) installed on a third-party mobile device which receives and displays real-time patient data from a continuous glucose monitor (CGM).
    - Regulation 862.1350; Product Code PJT: Continuous Glucose Monitor Secondary Display
    - The apps were later down-classified to a Class II device exempt from premarket clearances. Similar technologies (e.g., MiniMed by Medtronic K151236; 5/19/2015) are also exempt.
    - The Dexcom receivers, as opposed to the apps, were cleared through the PMA process (as the original Dexcom device)
      - P120005/S028 (01/23/2015) G4 platinum receiver update to include share to allow communication directly with the Dexcom mobile application installed on a user’s apple mobile device.
      - P120005/S033 (08/19/2015) G5 Mobile CGM System has Bluetooth built right in to the transmitter and sends glucose data directly to a smartphone, so users don’t have to carry a separate receiver device.
Thank You!

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VALUE IS THE NEW MANTRA

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December 16, 2015

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Medical Device Industry - 2015

• Projected CAGR next 10 years ~5%
• US will remain the most important market
  • Size, innovation, leadership / impact, pricing
  • US – home of 12 out of top 20 companies; EU - 7; Japan – 1
• Innovation is still strong
  • 3,000 – 3,500 FDA approvals / year
  • >150,000 health apps (but 90%<5,000 users)
• Continuing M&A
  • Start-ups / small companies are the primary innovation pipelines
  • >50% w/ FDA approval
  • ~25% CE
  • ~25% development stage
In the US Healthcare Expenses Keep Rising

Health Spending Per-Capita & GDP Per-Capita (2001-10)
But Higher Costs Do Not Provide Better Health
Cost Drivers

Source: BCBSMA Actuarial & Analytic Services.
Performance Pays Off

Cost

Heart Bypass Surgery

Average Hospital Costs

Patient Process Measure

Pneumonia

Average Hospital Costs

Patient Process Measure
Patient Protection and Affordable Care Act (2010)
Volume ➔ Value
Many Reforms and Initiatives

- **Accountable Care Organizations (ACO)** - shift from fragmented and inconsistent care to coordinated care and measured performance

- **Value-Based Purchasing (VBP) Program** - reward value and patient outcomes, instead of just volume of services

- **Reduced Payments for Hospital Acquired Conditions** - stop paying for certain conditions developed while the patient is hospitalized

- **Hospitals Readmission Reduction Program** – reduce payments to acute care hospitals with excess readmission

- **Payment Reforms** - incentivize Quality, not Volume
We Have a New Landscape

Volume based incentives → Value based / outcomes

Fee-for-service → Bundled care

Payers assume financial risk → Payers & providers

Brand defines quality → Quality defines brand

Devices selected by physician → System decisions
Value-Based Purchasing

Devices, Drugs, and Diagnostic pricing will be based on ability to remove costs from the system.
The Shift From ‘Doing More’ to ‘Doing Better’ Is Happening

- By 2018 50% of Medicare payments will move to alternative payment models like ACOs and bundled payment programs.

- By 2018 90% of all payments will be linked to quality or value
- Within 5 years fee-for-service will decrease from 56% to 32%

- VBP (2015):
  - 1,714 hospitals will have their Medicare payments boosted (1,251 in 2014)
  - 1,375 hospitals will have their Medicare payments reduced

- 2012 – hospital Medicare readmissions declined by 150,000
What’s Next? Money Back Guarantee?

Changes in reimbursement models are rippling out to manufacturers of drugs and devices.

“It is inevitable that drug and device makers’ reimbursement will eventually be tied to results. If that’s the way the hospitals and doctors are going to be paid, then the people they do business with have to be prepared to get paid that way as well.”

- Humana – 13 risk-sharing agreements with pharma companies (cancer, MS, diabetes, etc.)
- UnitedHealth – pay-for-performance deals for a new $1,000 /pill hepatitis C drug
- ICU Medical promises that its connectors for central-line catheters will reduce occlusions. Pay hospitals back if they don’t.
- St. Jude will refund 45% of a cardiac resynchronization device cost if patients require corrective surgery.
While Healthcare Markets Expand, Time to Clinical Adoption Continues to Increase
What’s going on?

- Resistance to change
- Greater competition
- Providers are vested in current technologies and practices
- Multiple decision makers with conflicting interests
- Changing economic incentives
- Evidence-based medicine... looking for more data
- Slow acceptance by payers
- Incremental features not justifying change
- Politics
Longer Time-To-Adoption Has Considerable Implications

- Delayed revenue
- Need for additional funds and financing rounds
- Valuations are negatively impacted
- Business development initiatives are delayed
- Increased risk of new competitors

Fewer make it

Takes longer

More barriers
Moore's Technology Adoption Life Cycle

How do you create a beachhead to cross the chasm?

Growth Profits

Techies Visionaries
Innovators Early Adopters

The Chasm

Pragmatics
Early Majority

Conservatives
Late Majority

Laggards
Late Minority

- Clinical Efficacy
- Clinical Pathways
- Pricing / Reimbursement
- Operating Model
When Are We Ready to Launch Sales?

Adoption of new technologies will require manufacturers to

- Ensure that the new device or drug is well integrated with workflow practices
- Demonstrate the value of the new products for healthcare providers and insurers
- How much money does the new drug / device save compared with other treatment options?
- Understand and demonstrate how much value a new device adds in terms of patient outcomes, and how does this compare with other alternatives?
Beware of the Myths

• We will do the studies needed to get FDA / CE approvals and the early customers will do the rest…

• We are not good at marketing, so once we get the 510k / CE we will sign the right distributor…

• A great product will sell itself…

• We do not need a Business Plan…

• Once we get money we will do the right things…

• We don’t have money, we need to be creative…