New Thinking at the FDA – Back to Basics

The Key – **Risks** (and Benefits)

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Zvi Ladin, Ph.D.

Principal

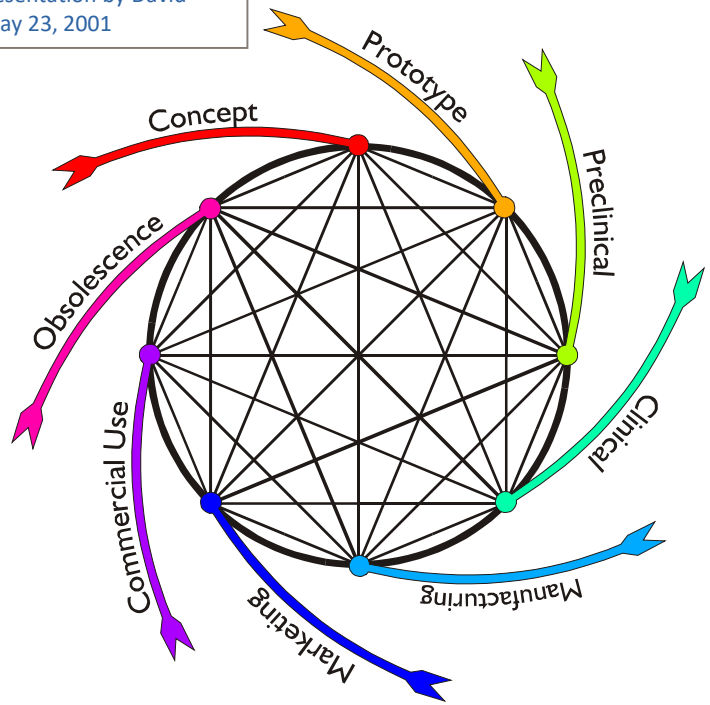
Boston MedTech Advisors

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

From FDA Presentation by David Feigal, MD May 23, 2001



- 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

UPI

HOME / SCIENCE NEWS

Medtronic pacemaker recall announced

WASHINGTON, June 11 (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.

December 16, 2011

The New York Times

Heart Device Parts Recalled

St. Jude Medical said on Thursday that its Riata 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.

WebMD

Recall of Defective Glucose Test Strips

Dec. 22, 2010 -- The FDA says it is working with Abbott Diabetes Care to recall 359 million defective glucose test strips -- sold under a variety of brand names -- that may make blood glucose levels look lowe than they really are.

drugwatch

Transvaginal Mesh Recall

In January 2012, the FDA issued postmarket surveillance study orders – called 522 orders– to all manufacturers of urogynecologic surgical mesh products. After the FDA issued the orders, some mesh manufacturers quietly withdrew their products from the market.

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.

Goals – Combine Clinical Research and Patient Care

Clinical Research

- Limited size
- Select sites
- Reductionist inclusion/exclusion
- Detailed information gathered
- Limited generalizability

Clinical Patient Care

- Large number of patients
- Various care venues
- Expansionist inclusion/exclusion
- Limited information gathered
- Generalizable

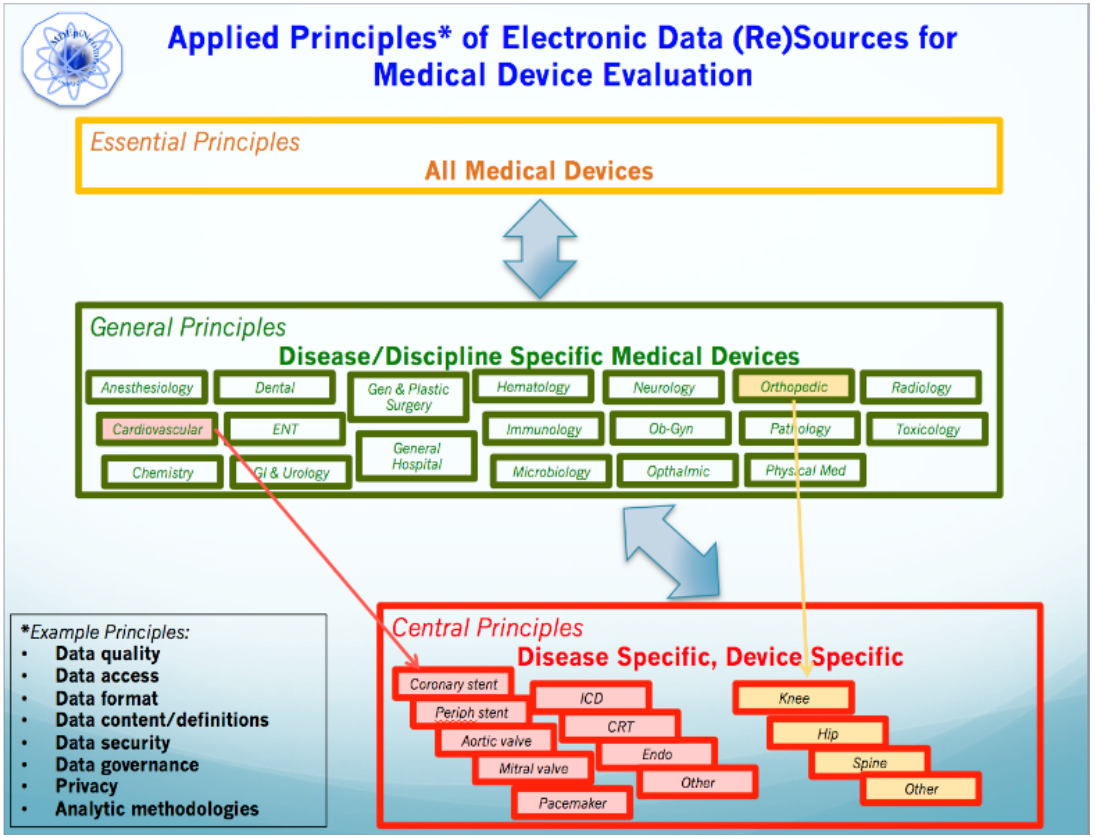
Development of **N**ational **M**edical **D**evice **E**valuation **S**ystem (**NMDES**)

- 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)
  - 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

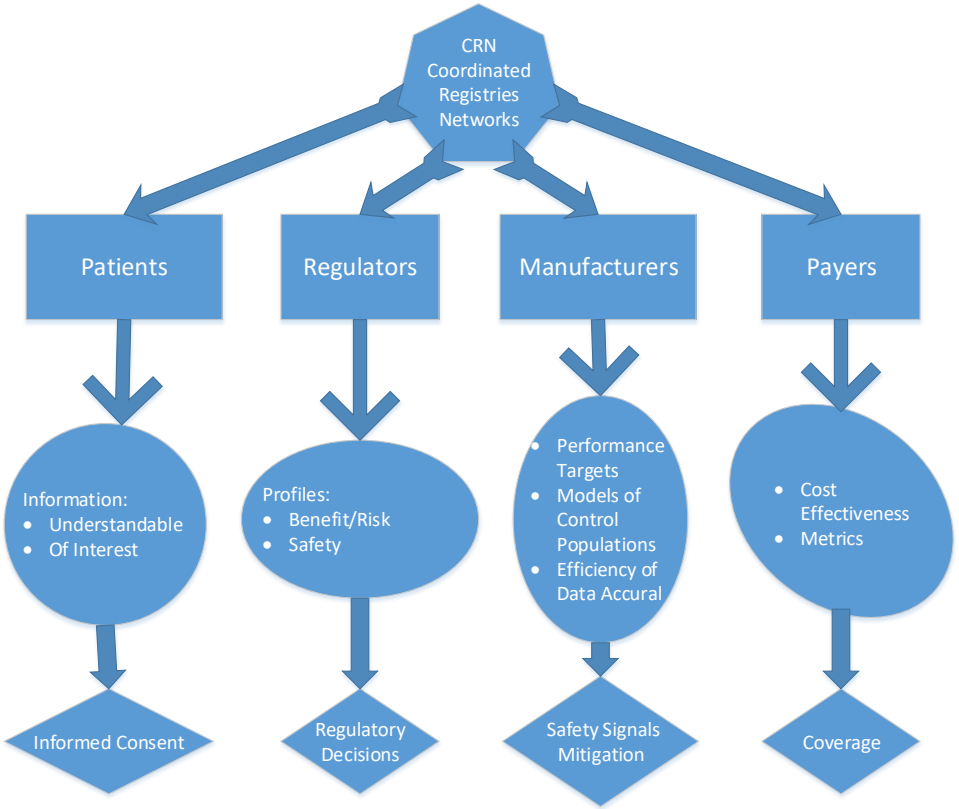
- **National Medical Evaluation System (FDA)**
  - **Source: Report – August 20, 2015**
  - Medical Device Registry Task Force & Medical Devices Epidemiology Network
- Recommendations
  - Multi-pronged approach – support different stakeholders
  - **Electronic Health Records (EHR)** – key for implementation
  - **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**

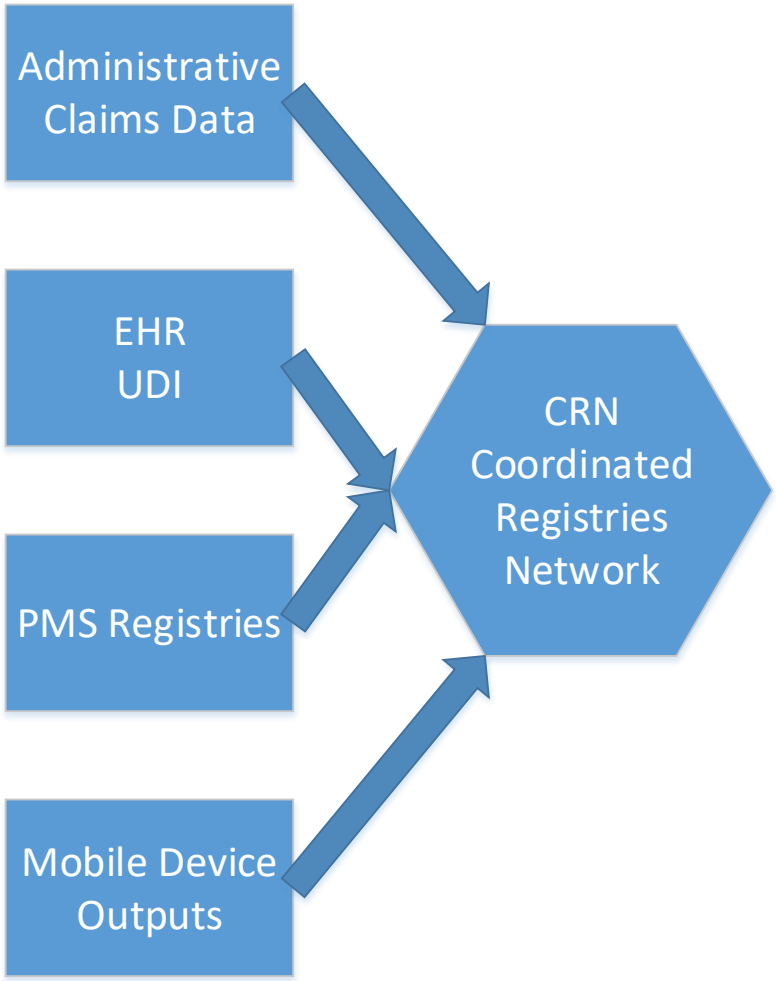
New Paradigm for PMS* – National Device Evaluation System



- 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."
- Guidance document (9/25/2013) focused on a risk-based approach.
  - **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
  - **Medical device data systems (MDDS)** (2/9/2015): **Deregulated all MDDS**, medical image storing devices and medical image communication 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!

Contact information:

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