CRNs as Foundational Blocks of the National Evaluation System for Medical Devices: A Call to Action

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Summary

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3. FDA Investments and Paradigm Shifts
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2016 - 2017 CDRH Strategic Priorities

- Establish a National Evaluation System for Medical Devices
- Partner with Patients
- Promote a Culture of Quality and Organizational Excellence
GOAL
Increase Access to Real-World Evidence to Support Regulatory Decision Making

- By December 31, 2016, gain access to 25 million electronic patient records (from national and international clinical registries, claims data, and EHRs) with device identification
- By December 31, 2017, gain access to 100 million electronic patient records with device identification
2016-2017 CDRH Strategic Priority #1

GOAL
Increase Use of Real-World Evidence to Support Regulatory Decision Making

• By December 31, 2016, increase by 40 percent the number of premarket and postmarket regulatory decisions that leverage real-world evidence. (compared to FY2015 baseline)
• By December 31, 2017, increase by 100 percent the number of premarket and postmarket regulatory decisions that leverage real-world evidence. (compared to FY2015 baseline)
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
Foundational Work: 2010-2015

2010

2012

2015

2013

Recommendations for a National Medical Device Evaluation System
Strategically Coordinated Registry Networks to Bridge Clinical Care and Research

STRENGTHENING OUR NATIONAL SYSTEM FOR MEDICAL DEVICE POSTMARKET SURVEILLANCE

STRENGTHENING OUR NATIONAL SYSTEM FOR MEDICAL DEVICE POSTMARKET SURVEILLANCE
UPDATE AND NEXT STEPS
FDA Investments 2011-2015

UDI  Established a Unique Device Identification (UDI) System

50  Completed or engaged in over 50 projects, including the creation of new RWE data sources, demonstration of proof of concept for use of RWE, development and use of advanced analytics

$20,000,000  Invested over $20 million
MDEpiNet Efforts/RWE Work Streams

Infrastructure

- Registry Development
- National/International Consortia Development
- Electronic Device Data Capture (UDI)
- Task Force - Coordinated Registry Networks
- PASSION Initiative

Methods

- Active Surveillance
- Distributed Data Analysis
- Evidence Synthesis
- Claims Validation
- Linkage with other Data Sources
- Big Data Analytics

Patient Engagement

- Augmenting Registries with PROs and Explant Analysis for Precision Medicine
- Assessing Minimally Important Difference (MID) for orthopedics implants
- Patient and Family Engagement Committee
- Patient-led Device/Disease Specific Round Table

4/5/2016
Changing Evidentiary Paradigm for Development and Evaluation of Medical Devices

**From:**
One-directional Evidence Stream

- Preclinical
- Clinical

**To:**
Multidirectional Evidence Streams throughout the TPLC of device and its iterations

- Preclinical (bench testing, in vitro and in vivo models)
- Premarket studies (RCTs)
- Real World Evidence

**Big data analytics**

- Discovery → Implementation
- Evaluation
National System Paradigm Shift

Passive Surveillance / One off studies

Challenging to find right pre/post market balance without confidence in post-market data

Current

Parallel Track to Clinical Practice

Inefficient one-off studies

Active Surveillance/ Embedded Studies

Collect data during routine clinical care

National System

Leverage RWE to support regulatory decisions throughout TPLC

Shared system to inform the entire Ecosystem (Patients, Clinicians, Providers, Payers, FDA, Device Firms)
Early Successes

National registries are being leveraged for:
• 15 Post-Approval studies
• 1 Continued Access study
• 1 labeling extension study
• 7 Postmarket Surveillance Studies (522)

International Registries are being leveraged for:
• 3 post-approval studies

Active review/analysis of data (starting early 2016)
• Example: American College of Cardiology (ACC) will share data with FDA quarterly for review
• Separate studies are no longer required, providing additional value
Impact: Shifts in Cardiovascular Device Post-Approval Studies Since 2010

Number of expensive studies is decreasing; replaced by cheaper studies.

Data as of November 30, 2015.
AND MOVING TO PREMARKET: Predictable And Sustainable Implementation Of National (PASSION) Registries

- FDA grant to MDEpiNet to prototype premarket studies embedded in registries
- Develop operational and business model for sustainable infrastructure for national registries
- Prototype premarket studies embedded in registries in cardiovascular space (peripheral, coronary, electrophysiology, valve)
- PASSION is a model for how to successfully leverage RWE for premarket review.
PASSION Predictable And Sustainable Implementation Of National (PASSION) Registries

• Develop operational and business model for sustainable infrastructure for national registries
  – accommodate different stakeholders with different expectations who value different deliverables from any one medical device registry

  - Performing 4 pilot projects in cardiovascular space (peripheral, coronary, electrophysiology, valve)
  - Standardize core data elements for global case report form
  - Develop data extraction interoperability
  - Apply a coordinated registries network to a prospective clinical trial supporting a regulatory decision
Impact: Registry Data Reduces Premarket Review Time!

- P100041
  - Filed: Oct 2010
  - TVT Registry used for Postmarket Surveillance.
  - Approved 45 days ahead of MDUFA goal

- P100041/S039
  - Filed: Nov 2011
  - TVT Registry data used for premarket approval.
  - Approved 154 days ahead of MDUFA goal
In February 2015, the multi-stakeholder Planning Board, convened by 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
- Recommends as a core strategy to use registries linked to longitudinal data systems
- Sets out an organizational structure and directions for pilots
- Developed consensus of stakeholders
Medical Device Registry Task Force

In August 2015, the multi-stakeholder Registry Task Force issued a convened by Duke, report that:

• Builds on the core strategy of White Papers and Planning Board Report
• Provides a direction for the future of registries
• Describes the role registries in the evolving National Medical Devices Evaluation System – proposes the pilots
• Recommends the creation of Strategically “Coordinated Registry Networks” – CRNs
• Identifies 11 priority areas
TF Recommendations: Nomenclature for the National System

From:
“National Medical Device Surveillance System”

To:
“National Evaluation System for Medical Devices”
TF: Transforming Heterogeneity to Dimensionality

Current Model:  
*Idiosyncratic heterogeneity*
- Disparate data sources
- Disparate data quality
- Disparate data elements
- Disparate definitions

Analytic Methodologies:
- *Signals vs. Noise*
- Build stand alone RCTs
  - “Vanilla” populations
  - Expensive & slow
- *Pre- vs Post-market gaps*

National System Model:  
*True heterogeneity of clinical practice*
- Data sharing infrastructure across existing e-health systems
- Implement structured data sets
  - Core minimum data elements
  - Common definitions
  - Device-specific applications

Assignable dimensionality of outcomes:
- Benefit/risk
- Signal detection & mitigation
- Clinical practice = research data
Strategically Coordinated Registry Networks (CRNs)

Existing Predicates of Data Sharing Solutions

A. Linked to complementary data sources
B. Multiple source structured data extraction
C. Distributed data networks
Task Force Report: Priority Devices/Procedures

- Hip Replacement/Resurfacing
- Knee Replacement
- Vascular Procedures
- Spinal Fusion
- Coronary Stenting
- Spine Surgeries
- Peripheral Vascular Stenting
Orthopedic CRN - Foundational blocks

- International Consortium of Orthopedic Registries (ICOR)
- US-based orthopedic registries (ICOR-USA)
- Registry-led partnership/harmonization efforts
- BO-PIE surveillance/studies model
International Consortium of Orthopedic Registries (ICOR)

**Partnership:**
- 29 Registries, (8 contributing data)
  - Over 4,500,000 implants

**UDI Promotion:**
- Global Clinically-Meaningful Attributes Database for Hips and Knees

**Methods:**
- Common Data Model to combine and de-identify data

- Comparative effectiveness / safety studies used in pre/post balance reviews (27 published)
- Use in FDA mandated PAS
- Catalyzed the development of ICOR-USA and Ortho CRN
- Informed the International Medical Device Regulators Forum (IMDRF) Registry Working Group
- Serves as a model for new International Consortia of Vascular, Transcatheter Valve, and Breast Implant registries
Proposed BO-PIE Model within ICOR-USA

General System Principles
- Capacity to employ layers of Infrastructure and Methodologies
- Flexibility for utilization of all or a subset of registries
  - Linkages
  - Clinical and/or Patient Reported Outcomes
  - Short- or long-term

General Registry Requirements
- Completeness
- Quality
- Linkages
- Transparency
- Adjudication
- Monitoring
- Access

Minimum Registry Data Requirements

BO Surveillance Platform
- B-Baseline
  - 0-None
  - 1-Device + Demographics
  - 2-Device + Demographics + Risk Adjustment
- O-Clinical Outcomes
  - 0-None
  - 1-Revision
  - 2-Revision + Reason for Revision
  - 3- Revision + reason for Revision + Mortality

PIE Studies Platform
- P-PRO
  - 0-None
  - 1-Any Recognized PROM Instrument
- I- Imaging
  - 0-None
  - 1-X-Ray
  - 2-MRI or CT
  - 3-X-Ray and (MRI or CT)
- E-Explants
  - 0-None
  - 1-Access to Explants
NEMDS: Value Proposition

• **Patients** would have more timely access to safer, more effective devices

• **Clinicians** would have better and more timely information about the use of a given device in practice.

• **Hospitals, clinical practices, and integrated health systems** would benefit from improved quality, reliable assurances of safety, and, possibly, relief from multiple reporting requirements

• **Payers** would benefit from access to high-quality evidence on device performance in clinical practice, either alone or compared with other therapies
NEMDS: Value Proposition

- Device manufacturers would be able to provide high-quality evidence at lower cost and in less time to support premarket approval, clearance, and payer coverage, coverage with evidence development and reimbursement decisions, to enable informed decisions about when devices should be used in particular patients and how to mitigate risk across the device’s lifecycle, and to meet postmarket study and adverse event reporting requirements.

- In cases where the potential public health value of the device is high, some data that would otherwise be collected in the premarket setting could be responsibly collected postmarket instead, owing to strong assurances that additional postmarket data would be generated.

- The system may obviate the need for FDA premarket review of some device modifications because more timely and informative evaluations of the impact of those changes would occur in the course of routine data collection.

- In fact, the FDA has already taken some of these steps for a handful of device types.
Why CRNs?

• Building a de novo national system for devices:
  – Cost prohibitive
  – Diversity prohibitive
  – Perception prohibitive
  – Outdated by launch
• Of current & emerging e-health information sources (registries, EHRs, administrative, mobile apps, etc) registries provide most robust content & operational predicates
• No single registry suffices for benefit/risk & safety for all devices
• Strategic data sharing interoperability (linking) complementary e-health sources could mitigate single source deficiencies: CRNs
Why CRNs? Alignment with the Planning Board: 
*Foundation & first steps, not a final blueprint*

- Scalable system (strategic CRN) architecture:
  - Leverages existing systems & efficiencies
  - Staged implementation, beginning in selected priority device areas
  - Pilot projects portfolio: immediate device impact & re-useable partnering, data-sharing solutions
  - Re-use of solutions across device areas builds momentum & consistency
  - Preserves flexibility for customization across diversity:
    - specific devices & innovation areas
    - individual stakeholder needs
    - emerging health information technologies
- Actively promotes good will & partnering across medical device ecosystem
Why CRNs? Small steps to big changes

- Priority device focus
- Opportunistic, successful first steps
- Immediate device-specific & generalizable deliverables
- National System should actively catalogue lessons learned & data sharing solutions for use/re-use, accelerating development of CRNs in additional device areas
- Build momentum, consistency & confidence
Why RWE?

• More efficient and better quality virtual registries to support this paradigm shift
  – Standardization of electronic data capture, development of common data elements and accepted definitions to ensure high quality, timely data (Coordinated Registry Networks)
  – Develop routine access to data through data sharing agreements

• Ability to use innovative methodological approaches for studies
  – Registry-derived comparison groups, EHR-driven comparison groups, big data analytics
  – Nesting new clinical trials in registries (e.g., Safe STEMI for Seniors)
  – Link registries (national and international) with longitudinal data (claims, EHR, PCORNET)

• Robust regulatory apparatus that utilizes RWE to streamline device evaluation and support innovation
Thank you!

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