National Evaluation System for health Technology (NEST) : RWE and Beyond

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The table above shows an overview of the FDA's strategic priorities, including NEST, Registries, MDEpiNet, and IMDRF.
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: 2010-2016
1. Establish a National Evaluation System for Health Technologies

2. Partner with Patients

3. Promote a Culture of Quality and Organizational Excellence
2016-2017 CDRH Strategic Priority #1

GOAL 1. 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)
Overview

2016-2017 CDRH Strategic Priority #1
Goal 2.
Increase Access to Real-World Evidence to Support Regulatory Decision Making

Current Status

16 Registries + 3 international registry consortia >28 million records

Access established and demonstrated by our ability to query those data sets. (e.g. TVT, INTERMACS)
Overview
FDA Strategic Priorities

**NEST**
Registries
MDEpiNet
IMDRF

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**National Evaluation System for health Technology (NEST)**

**Vision**

**Foundational Work**

**Paradigm Shift**

**Selection of NEST/MDIC Coordinating Center**

**Planning Board Implementation Plan published**
Registries, Consortia and CRNs

Overview

FDA Strategic Priorities

NEST

Registries

MDEpiNet

IMDRF

National Medical Device Registry Task Force
CRNs

Linkages with Complementary Data Sources (EHR, Claims)
CRN Principles:

- Link complementary sustainable registries/e-repositories (Professional society registries, EHRs, VAMC, Claims data)
- TPLC as a true continuum of structured “real world” evidence
- “Dual purpose” existing site-base work flow
Strategically Coordinated Registry Networks (CRNs)

Existing Predicates of Data Sharing Solutions

A. Linked complementary registries

B. Multiple source structured data extraction

C. Distributed data networks
Embedding a randomized clinical trial into an ongoing registry infrastructure: Unique opportunities for efficiency in design of the Study of Access Site for Enhancement of Percutaneous Coronary Intervention for Women (SAFE-PCI for Women)

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Evolving CRNs

• Ortho CRN
• Vascular CRN - VISION
• Neuro CRN - DAISI
• Robotic Surgery CRN
• HIFU CRN
• GI CRN
• Women’s Health CRN
Medical Device Evaluation Paradigm Shift: Today and Tomorrow

Passive Surveillance
- Challenging to find right pre/post market balance without confidence in post-market data
- Inefficient one-off studies
- Parallel Track to Clinical Practice
  - Current

Active Surveillance
- Leverage RWE to support regulatory decisions throughout TPLC
- National System
  - Collect data during routine clinical care
  - Shared system to inform the entire Ecosystem (Patients, Clinicians, Providers, Payers, FDA, Device Firms)
Shifts in Cardiovascular Device Post-Approval Studies Since 2010

Number of expensive studies is decreasing; replaced by less costly studies.
Another way to look at registry embedded studies: LEVI’S

- L
  - Leveraged
- E
  - Embedded
- V
  - Valuable
- I
  - Inexpensive
- S
  - Sound Science

Adapted from Michael Lauer, NIH, 2015
Modeling return-on-investment for a regional hip and knee replacement quality improvement collaborative

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In 5 Countries Demonstrates The Potential To Use Outcome Data To Improve Health Care’s Value

ABSTRACT As health care systems worldwide struggle with rising costs, a consensus is emerging to refocus reform efforts on value, as determined by the evaluation of patient outcomes relative to costs. One method of using outcome data to improve health care value is the disease registry. An international study of thirteen registries in five countries (Australia, Denmark, Sweden, the United Kingdom, and the United States) suggests that by making outcome data transparent to both practitioners and the public, well-managed registries enable medical professionals to engage in continuous learning and to identify and share best clinical practices. The apparent result: improved health outcomes, often at lower cost. For example, we calculate that if the United States had a registry for hip replacement surgery comparable to one in Sweden that enabled reductions in the rates at which these surgeries are performed a second time to replace or repair hip prostheses, the United States would avoid $2 billion of an expected $24 billion in total costs for these surgeries in 2015.
A Registry-Based Randomized Trial Comparing Radial and Femoral Approaches in Women Undergoing Percutaneous Coronary Intervention

The SAFE-PCI for Women: Comparison of Radial Versus Femoral Access for Percutaneous Coronary Intervention—Enhancement of PCI for Women Registry

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and a database that is compliant with the U.S. Food and Drug Administration guidelines on electronic records (30), was ~$5 million, which is far less than a comparably sized trial would have cost without the NCRI model. This model is an ideal platform for more efficient and productive investigational drug or device studies. Conducting clinical trials for innovative new therapies is increasingly becoming cost prohibitive; in this context, the NCRI model appears to be a promising platform for future clinical investigations (31).
Registry Development
National/International Consortia Development
Electronic Device Data Capture (UDI)
Task Force - Coordinated Registry Networks
PASSION Initiative

Active Surveillance
Comparative Effectiveness
Evidence Synthesis
Claims Validation
Linkage with other Data Sources
Big Data Analytics

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

MDEpiNet
Portfolio

Infrastructure

Methods

Patient Engagement
International Consortium of Orthopedic Registries (ICOR)

- Comparative effectiveness / safety studies (27 papers published in JBJS)
- 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

**Partnership:**
- 29 Registries, (8 contributing data)
- Over 5,200,000 implants

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

**Methods:**
- Common Data Model to combine and de-identify data
In response to MDEpiNet Proposal, IMDRF established the Registry Working Group:

- Phase 1. Essential principles for linking electronic patient, device and outcome registries and/or related data repositories or identifiers such as unique device identifiers, including the principles behind data access, security, informatics formats, governance and other key areas related to global regulatory applications for medical device evaluation.

- Phase 2. Essential principles related to optimal methodologies for analysis of heterogeneous data sources applied to medical device safety signal detection, performance and reliability.
“Organized system that continuously and consistently collects relevant data in conjunction with routine clinical care, evaluates meaningful outcomes and comprehensively covers the population defined by exposure to particular device(s) at a reasonably generalizable scale (e.g. international, national, regional, and health system)’ with a primary aim to improve the quality of patient care”. 
Key Registry Attributes

- **DEVICE**: The registry contains sufficient information to uniquely identify the device. Ideally, the unique device identifier would be included, but when the UDI is not available, the registry would include a combination of identifiers (catalog, number, manufacturer, description) that, in combination, will assist in uniquely identifying the device.

- **QUALITY IMPROVEMENT SYSTEM**: The registry is part of a health care delivery quality improvement system or evolving into one as device technologies are diffused into practice and need continuing evaluation (including outlier identification).

- **BENEFICIAL CHANGE**: The registry has established mechanisms to bring about beneficial change in health care delivery through stakeholder participation, ownership and integration into the relevant health care systems.

- **EFFICIENCY**: The registry is embedded in the health care delivery system so that data collection occurs as part of care delivery (i.e., not overly burdensome, not highly complicated, not overly costly, etc.) and integrated with work flow of clinical teams.

- **ACTIONABLE DATA**: The registry provides actionable information in a relevant and timely manner to decision makers.

- **TRANSPARENCY**: The governance structure, data access, and analytical processes of the registry are transparent.

- **LINKABILITY**: Information in the registry can be linked with other data sources for enhancement including adequate follow up achievement.

- **TOTAL DEVICE LIFE-CYCLE**: The registry can serve as infrastructure for seamless integration of evidence throughout the device life cycle.
### Phase 1: Key Recommendations

1. Use of controlled vocabularies (standardized data dictionaries)

2. Use of a common data model (e.g., Observational Medical Outcomes Partnership Common Data Model, at: [http://omop.org/CDM](http://omop.org/CDM))

3. Inclusion of device-related performance and device outcomes information

4. Implementation of a data quality plan for the evaluation and assurance of the quality and provenance of the data

5. Governance that anticipates the conduct of analyses across different types of analysis frameworks
The process should exist by which important information and data (on either a summary level or observation level), will be shared in a structured fashion by regulators across multiple countries. This process should be agreed upon before analyses are performed;

Where appropriate, registry structure should be leveraged to efficiently answer questions that would have historically been addressed via more resource intensive legacy tools (e.g. PASS studies in EU; 522 Studies in US);

Registries should be exploited to facilitate the conduct of clinical trials both premarket and postmarket;

Separation within and between country variation for analysis is necessary in order to ensure effective individual and international decision making. Explicit modeling to help determine factors influencing the within- and between-country variability would be useful;

Pre-specification of analyses that could drive regulatory decisions is essential. Beyond the direct specification of analyses, effort should be devoted towards construction of a verification and reproducibility plans for findings from the analyses driven by models;

Further consideration should be given to assessing optimal role of spontaneous adverse event reporting in the context of international Coordinated Registry Networks (iCRNs).
Thank you!

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