Leveraging Real World Evidence to Get Better, Faster, Cheaper Medical Devices for Physicians and Patients

Major initiatives:

- **Medical Device Epidemiology Network (MDEpiNet)**
- **Registry Assessment of Peripheral Interventional Devices (RAPID)**
- **SFA-Popliteal Evidence Development (SPEED)**

October 12, 2018 - 1:00 pm  U.S. Eastern Time

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**Terrie Reed**, MSIE, Senior Advisor for UDI Adoption, US Food & Drug Administration

**Roseann White**, MA, Director of Innovative Clinical Trial Statistics, Duke Clinical Research Institute
Paradigm shift in Healthcare
Purpose

Webinar
• Educate viewers about MDEpiNet, RAPID, and SPEED

MDEpiNet RAPID
• Better, Faster, Cheaper devices to patients’ bedsides
  • FDA, clinician, and manufacturer partners benefit from the use of real world evidence
  • More partners = Greater diversity = Better data and results
  • Medical device manufacturers can leverage real world data in RAPID Phase III
Medical Devices: “The Opportunity”

- **Capture** “real world evidence” in order to evaluate pre- and post-market safety and effectiveness of medical treatment
- **Develop** analytical methodologies for device evaluation
- **Generate** guiding principles and clear data governance
- **Build** infrastructure to share best practices amongst diverse stakeholders and merge data sources for better interoperability
- **Demonstrate** more effective capture and reuse of UDI across supply chain, clinical, and analytical systems
Medical Device Epidemiology Network (MDEpiNet)
What it is:
- A public-private partnership, started in 2010, with stakeholders from FDA, private industry, academia, professional organizations, etc

**Purpose**: Bring together leadership, expertise, and resources to support a national medical device evaluation system

**Mission**: Advance national and international infrastructure for patient-centered regulatory science, surveillance and quantitative methodology

**Goal**: Optimize evidence generation, appraisal, and synthesis for medical device Total Product Lifecycle (TPLC) evaluation
Value of Device Lifecycle and Evaluation

- Conducting Studies
- Developing Methodology
- Building Infrastructure

Faster, more cost-effective studies
Improving patient-centered outcomes
Better, safer devices
Benefits of MDEpiNet for Patients, Clinicians, Industry, Regulatory Agencies

Better product
- Better devices, faster to bedside for patients
- Improved pre-/post-market balance

Increased information
- Information on device risk/benefit
- Comparative effectiveness, cost-effectiveness
- Historical data (modeling; performance goals and criteria)
- Best practice guidelines
- Increased data sets for greater accuracy

Greater efficiency
- Interoperable collection and exchange of electronic health data
- Reduced regulatory burden
- Leveraging existing data for device evaluation
Registry Assessment of Peripheral Interventional Devices (RAPID)
Registry Assessment of Peripheral Interventional Devices (RAPID)

- The MDEpiNet RAPID project is designed to advance the foundational elements of the approach for the evaluation of medical devices used to treat and manage peripheral artery disease.
- RAPID is an archetype of the total product lifecycle ecosystem.
- It is one of a series of projects initiated to advance and demonstrate the interoperable flow of data across electronic health information systems.
- Is fundamental to the basis of the development of the National Evaluation System for Health Technology (NEST).
- A demonstration project of MDIC/NEST, a public-private partnership.
RAPID Leadership Team

Principal Investigators
- Jack Cronenwett, MD, Society of Vascular Surgery, Vascular Quality Initiative
- Pablo Morales, MD, United States Food and Drug Administration
- Robert Thatcher, 4C Medical Technologies

Key Advisors
- Mitch Krucoff, MD, Duke Clinical Research Institute
- Danica Marinac-Dabic, MD, Ph.D., MMSC, United States Food and Drug Administration

Project Management and Informatics Support
- Duke Clinical Research Institute
- Weill Cornell Department of Healthcare Policy and Research
RAPID Partners

Medical Societies / Registries

- American College of Cardiology (ACC)
- National Cardiovascular Data Registry (NCDR) – Peripheral Vascular Intervention (PVI)
- Society of Interventional Radiology (SIR)
- National Interventional Radiology Quality Registry (NIRQR)
- Society for Vascular Surgery (SVS)
- Vascular Quality Initiative (VQI) – Peripheral Vascular Intervention (PVI)
- International Consortium of Vascular Registries (ICVR)

Government Agencies

- FDA (Center for Devices and Radiological Health (CDRH) and Center for Drug Evaluation and Research (CDER))
- Agency for Healthcare Research and Quality (AHRQ)
- Centers for Medicare and Medicaid Services (CMS)
- Department of Defense (DOD) Healthcare Resources
- Office of the National Coordinator (ONC)
- National Heart, Lung and Blood Institute (NHLBI)
- National Library of Medicine (NLM)
- Japan’s Pharmaceuticals and Medical Devices Agency (PMDA)
RAPID Partners (cont.)

Companies / Organizations

- 4C Medical Technologies, Inc.
- Aorta Medical, Inc.
- Boston Biomedical Association
- Cerner
- Cognitive Medical Systems
- Deloitte Healthcare
- Device Events
- Epic
- First Databank, Inc.
- Global Healthcare Exchange
- Global Medical Device Nomenclature (GMDN)
- Healthjump, Inc.
- MedStreaming/M2S
- MDIC/NESTcc
- INC Research
- IQVIA (formerly Quintiles)
- PCPI
- Pharm3r
- Ultamed Corp
RAPID Funders
RAPID Goals: Phase I

- **Phase I:** Identify minimal set of core data elements for registry assessment of lower extremity arterial devices, including methods to identify specific devices being used.

- **Phase II:** Demonstrate the feasibility of data extraction interoperability across registries and hospital EHRs that provide patient-level data for core data elements.

- **Phase III:** Use a coordinated registries network (CRN) for studies supporting a regulatory decision.
RAPID Phase I: Delivered

- **Phase I**: Identify minimal set of core data elements for registry assessment of lower extremity arterial devices, including methods to identify specific devices being used – *Completed!*
- Meta-data of the 100 core data elements include:
  - Data element label (e.g. Modified Rutherford Category; wound grade)
  - Data element definition
  - Value set
  - Definitions of the elements of the value set
  - Reference source

Download RAPID Phase I Core Data Elements at:
RAPID Phase I: Delivered (cont.)

Core Data Elements
- 100 “key core data elements,” including UDI, covering patient characteristics, clinical descriptors, device descriptors, lesion descriptors, etc., as published in *Journal of Vascular Surgery*

Use Cases for Core Data Elements
- Infrastructure facilitates interoperability between registries, EHRs, and other data sources

Workflow Diagrams
- Point of care, total product lifecycle and registry-based clinical studies/trials

GUDID (Global Unique Device Identifier Database) Project Summary
- Key learnings about use of GUDID data
RAPID Goals: Phase II - Completed

- Phase I: Identify minimal set of core data elements for registry assessment of lower extremity arterial devices, including methods to identify specific devices being used.

- **Phase II:** Demonstrate the feasibility of data extraction interoperability across registries and hospital EHRs that provide patient-level data for core data elements.

- Phase III: Use a coordinated registries network (CRN) for studies supporting a regulatory decision.
Phase II Stakeholder Working Groups

1. Informatics, Interoperability & Global Unique Identifier (GUDID)
2. Governance, Access, Data Sharing
3. Protocol Development
   a) Statistics
   b) Industry
   c) Clinician
4. Educational Outreach
SFA-Popliteal Evidence Development (SPEED)

http://aicdheart.com/patient_education/heart_HTML_scaleable/heart/fempop.htm
http://www.yoursurgery.com/ProcedureDetails.cfm?BR=5&Proc=33
SFA-Popliteal EvidencE Development (SPEED)

RAPID Phase II

Why SPEED?

- Multiple devices currently in use, with new drug-coated and other technologies in pipeline
- Expansion of current labeling for appropriate use
- Provide additional real world evidence for clinical and regulatory decision making
- Modernize objective performance criteria (OPC) for SFA-POP devices

Goals of SPEED:

- Device-specific data for companies that wish to expand indications for use of current devices
  - Line-by-line data to allow propensity matching to establish non-inferiority of new device compared with contemporary treatment of similar patients and lesions
  - Contemporary OPC for percutaneous/peripheral vascular intervention (PVI) treatment
    - Dynamic OPCs depending on patient, lesion, and treatment type characteristics
What is Vascular Quality Initiative (VQI)?

- VQI Mission: Improve the care of vascular patients.
- Registry sponsored by the Society for Vascular Surgery
- VQI includes over 450 sites and 450,000 patients
- Incorporated RAPID core data elements into its Peripheral Vascular Intervention (PVI) data
- Data source for RAPID/SPEED

458 Centers, 46 States + Canada
Benefits of Real World Evidence

**Better**
- Enhance safe, effective, and patient-centric outcomes
- Inform users and patients of real world performance
- Improve relevance over traditional post-market studies

**Faster**
- Expand indications for new patient populations
- Reduce time to patient access

**Cheaper**
- Alleviate burden on clinical research enterprise (pre- and post-market)
- Lower cost of clinical evidence generation
Global Benefits

Harmonization of various registries
- Incorporate RAPID / SPEED common data elements in all national registries
- When national registries do not exist, utilize data from other registries to gain regulatory approval or label expansion

Elimination of small clinical trials with no statistical significance
- Leverage existing patient data to gain regulatory approval
- When eliminated as an approval requirement, reduces time to market
Results of SPEED Analysis
Roseann White, MA, Director of Innovative Clinical Trial Statistics, Duke Clinical Research Institute
Objective Performance Criteria

• Determine the minimum acceptable success rate for demonstrating device effectiveness

• Determined after there is a large accumulation of performance data for the type of device

• Determine the minimum acceptable success rate for a device based on the trial population e.g. provide an OPC calculator

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• Detailed Statistical Analysis Plan (SAP) developed
Analysis Populations

- For each vessel-based subgroup, an objective performance criteria (OPC) will be developed for the following sets of procedures:
  - All patients with any of the following: PTA, Stent, or Atherectomy
  - Percutaneous Transluminal Angioplasty (PTA) only
  - Stent with or without PTA
  - Atherectomy with or without PTA
  - Stent + Atherectomy
Dataset for SPEED Analysis

- 30,899 patients
  - 25,077 patients with 1 procedure
  - 5,822 patients with more than 1 procedures

- 38,344 procedures

- 26,389 procedures

- 22,362 SFA
- 11,001 POP
Endpoints of interest

**Endpoints of interest**

**Covariates of Interest**
- Patient level
- Limb level
- Lesion level
- Artery level

**Outcomes of Interest**
- Mortality, any cause
- Major amputation
- Amputation free survival (AFS)
- Target lesion revascularization (TLR)
- Open surgery
- Target lesion occlusion
- Target Vessel Revascularization
- Clinical challenges
Procedure Data Acquired

- Procedure A - three lesions treated: SFA (Right-R), SFA (R), POP (R)
- Procedure B - two lesions treated: SFA (R), SFA (R)
- Procedure C - two lesions treated: POP (R), POP (Left-L)
- Procedure D - three lesions treated: SFA (R), SFA (R), POP (L)
- Procedure E - three lesions treated: SFA (R), SFA (L), POP (L)
Results of SPEED

- TBD – use graphic/pivot table
Unique Device Identifier / Global Unique Identifier (GUDID)

Terrie Reed, MSIE, Senior Advisor for UDI Adoption, US Food and Drug Administration
How important is it to identify an Implant?

Company Announcement

When a company announces a recall, market withdrawal, or safety alert, the FDA posts the company's announcement as a public service. FDA does not endorse either the product or the company.

Pepperidge Farm® Announces Voluntary Recall of Four Varieties of Goldfish® Crackers

For Immediate Release  July 23, 2018

Contact

Consumers
Customer Service
800-679-1791

Media
Bethridge Toovell
Bethridge_Toovell@PepperidgeFarm.com
203-846-7136

Announcement

Pepperidge Farm has been notified by one of its ingredient suppliers that whey powder in a seasoning that is applied to four varieties of crackers has been the subject of a recall by the whey powder manufacturer due to the potential presence of Salmonella. Pepperidge Farm initiated an investigation and, out of an abundance of
Consumers can make decisions within days

Company Announcement

When a company announces a recall, market withdraw announcement as a public service. FDA does not end

Pepperidge Farm® Anno of Four Varieties of Gold:

For Immediate Release

July 23, 2016

Contact

Consumers
Customer Service
800-679-1791

Announcement

Pepperidge Farm has been powder in a seasoning that subject of a recall by the wt Salmonella. Pepperidge Fa
UDI in RAPID: Improve decision making with better UDI data

Phase II Overview

1. Objective
   a) To improve UDI capture/utilization and broaden its impact
   b) Demonstration Project → Use findings and partnerships built in previous RWE efforts to define a Lean study of UDI workflows

2. Methodology
   a) FDA, manufacturers, and researchers conduct a joint workflow and data science analysis to assess existing capture of device data recommend improvements
   b) Conduct a partner-based quality improvement (LEAN) study of workflow associated with the recording of core Phase I data (including UDI) into a hospital EHR, the transfer of UDI and other data into a PAD registry, and pulling of the data from the registry to meet a specific device evaluation requirement
Impact

1. **Expected Research Outputs**
   a) Identification of hospital supply chain, clinical, and registry device identification requirements
   b) General method to conduct data science analysis of a particular device type to improve UDI capture at point of care
   c) Measurable improvement in quality of GUDID data, incorporation into user datasets, and evaluation of impact on clinical and regulatory decision making

2. **Intended Impact for NESTcc**
   a) Improved understanding of the device clinical, supply chain and research requirements for GUDID data
   b) Improvements in partner relationships across UDI implementers – Industry, healthcare, supply chain, researchers
   c) Generalizable methodology that can be applied to other health partners and registries
   d) Identification of GUDID data for improvement and UDI linkages that can be source of further study
RAPID Phase III: Future Goals

• Phase I: Identify minimal set of core data elements for registry assessment of lower extremity arterial devices, including methods to identify specific devices being used.

• Phase II: Demonstrate the feasibility of data extraction interoperability across registries and hospital EHRs that provide patient-level data for core data elements.

• Phase III: Use a coordinated registries network (CRN) for studies supporting a regulatory decision.
The Goal: **Better, Faster, Cheaper Devices to Patients’ Bedside**

- FDA, clinician, and manufacturer partners benefit as well
- More partners = Greater diversity = Better data and results
- Medical device manufacturers can leverage real world data and clinical trial evidence in RAPID Phase III
Call to Action

• **Device manufacturers: Utilize** real world evidence in evaluating and releasing new devices and expanding indications.

• **Clinicians: Contribute** to the generation of real world evidence.

• **Regulatory bodies: Increase use** of real world evidence and patient level data for device approval.
Organizations that provided images in this presentation

- Boston Scientific Corporation
- Cook Medical
- CRBard, Inc.
- Cardiovascular Systems, Inc.
- Duke Clinical Research Institute
- EPicardio
- Intact Vascular, Inc.
- Medtronic
- Society for Vascular Surgery
Web Site and Contact Information

- Join us by emailing: MDEpiNet@dm.duke.edu / sarah.palmer@duke.edu
- Web sites:
  - MDEpiNet: http://mdepinet.org
  - RAPID Project: http://mdepinet.org/rapid/
  - NEST CC Demonstration Projects: https://nestcc.org/demonstration-projects/
  - FDA: https://www.fda.gov/MedicalDevices/ScienceandResearch/EpidemiologyMedicalDevices/MedicalDeviceEpidemiologyNetworkMDEpiNet/default.htm
RAPID Publications and Guidance

• Journal of Vascular Surgery, Feb. 2018
  • https://www.ncbi.nlm.nih.gov/pubmed/29389426

• Circulation Journal (Japan), 2018
  • https://www.jstage.jst.go.jp/article/circj/82/2/82_CJ-17-1156/_article/-char/en

• Endovascular Today, Oct. 2017

• FDA Guidance, Aug. 2017

• Endovascular Today, Aug. 2016