US Regulatory and Marketing Barriers for Medical Devices

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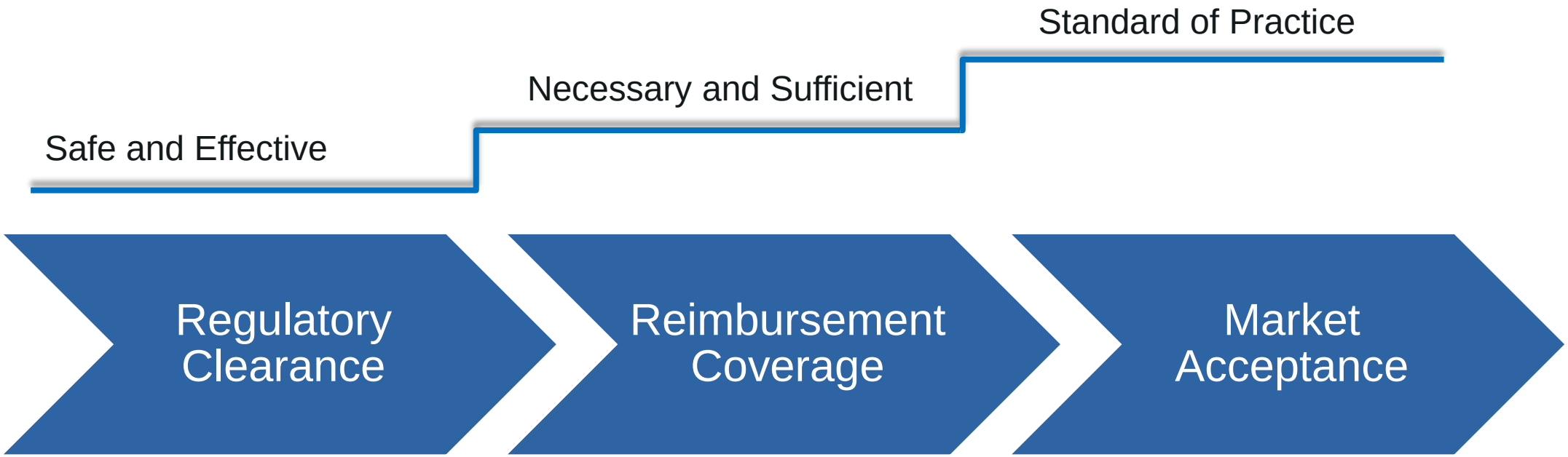
The Old Linear Paradigm



Small-Size Clinical Trials

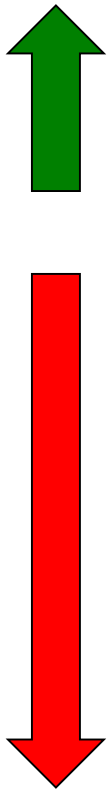
Post-Market Surveillance Studies

Marketing ‘Studies’

US Medical Device Market – Perceived Problems (2010 and beyond)

Complaint

- Early Clinical Testing
- Regulatory Hurdles
- Regulatory-Related Costs
- Post-Market Failures

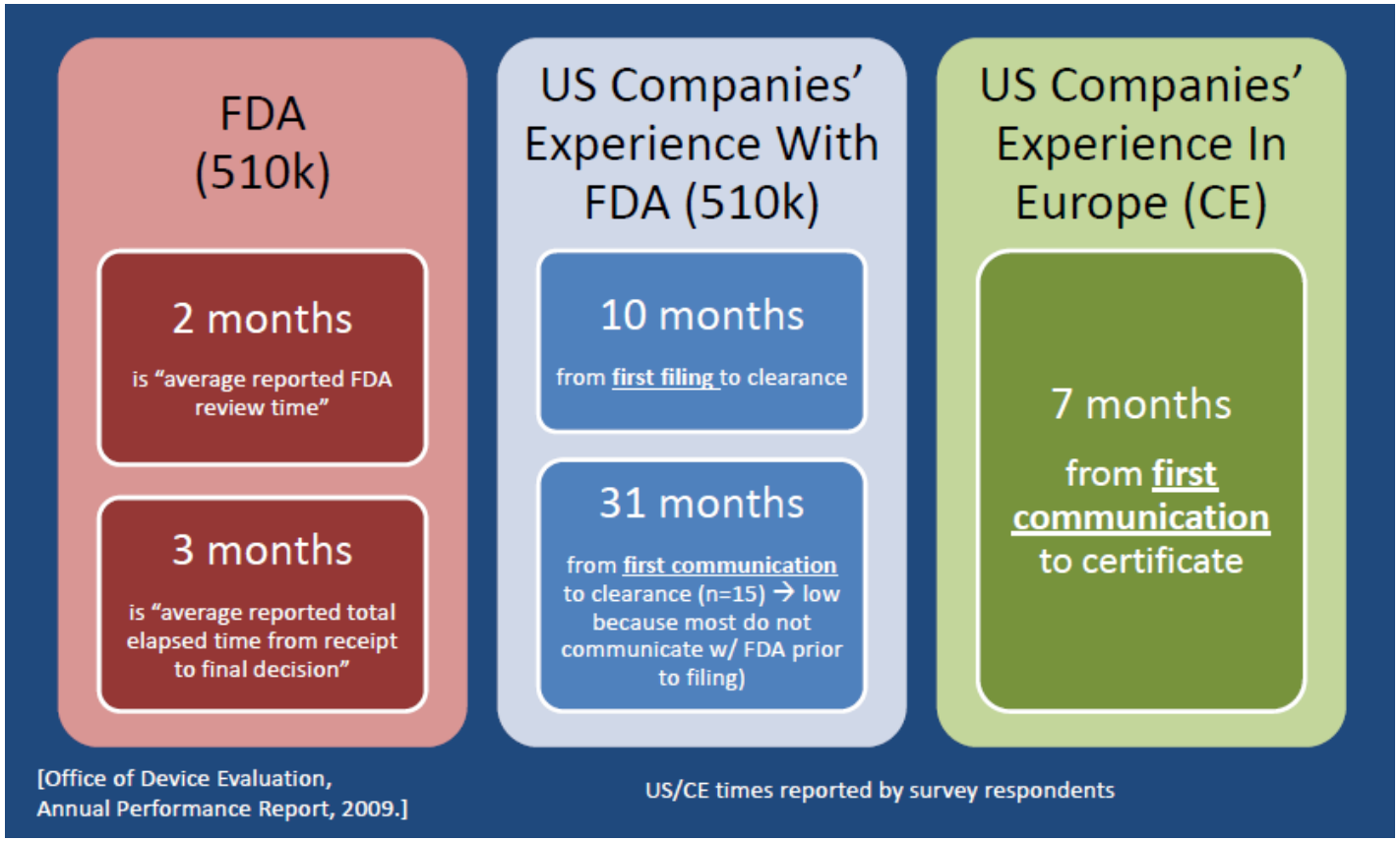


FDA Response

- ✓ Improve FIH (First in Human) Access
- ✓ Streamline Review Process
- Dispute
- ❑ NMDES…….

510(k) & CE timelines in US & Europe (**2010 Industry View!**)

Reported FDA transit times underestimate actual regulatory delay



Source: Makower, J. FDA Impact on U.S. Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies, November 2010

Cost of Concept to Clearance / **2010 Industry Perspective**

- Average to clear 510(k) – $31 million*
  - $24 million on FDA-dependent/related

- Average to clear PMA – $94 million*
  - $75 million spent on FDA-dependent/related aspects

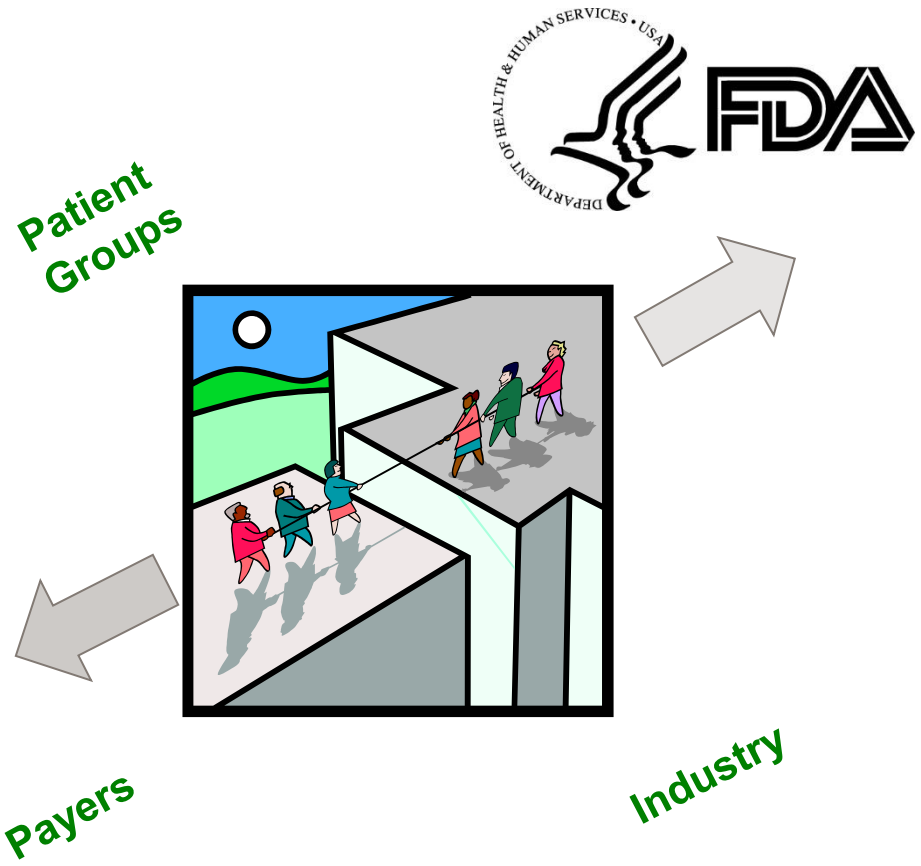
* Does not include reimbursement approval and sales/marketing costs.

FDA Disputes Both Values!

Source: Makower, J. FDA Impact on U.S. Medical Technology Innovation: A Survey of Over 200 Medical Technology Companies, November 2010

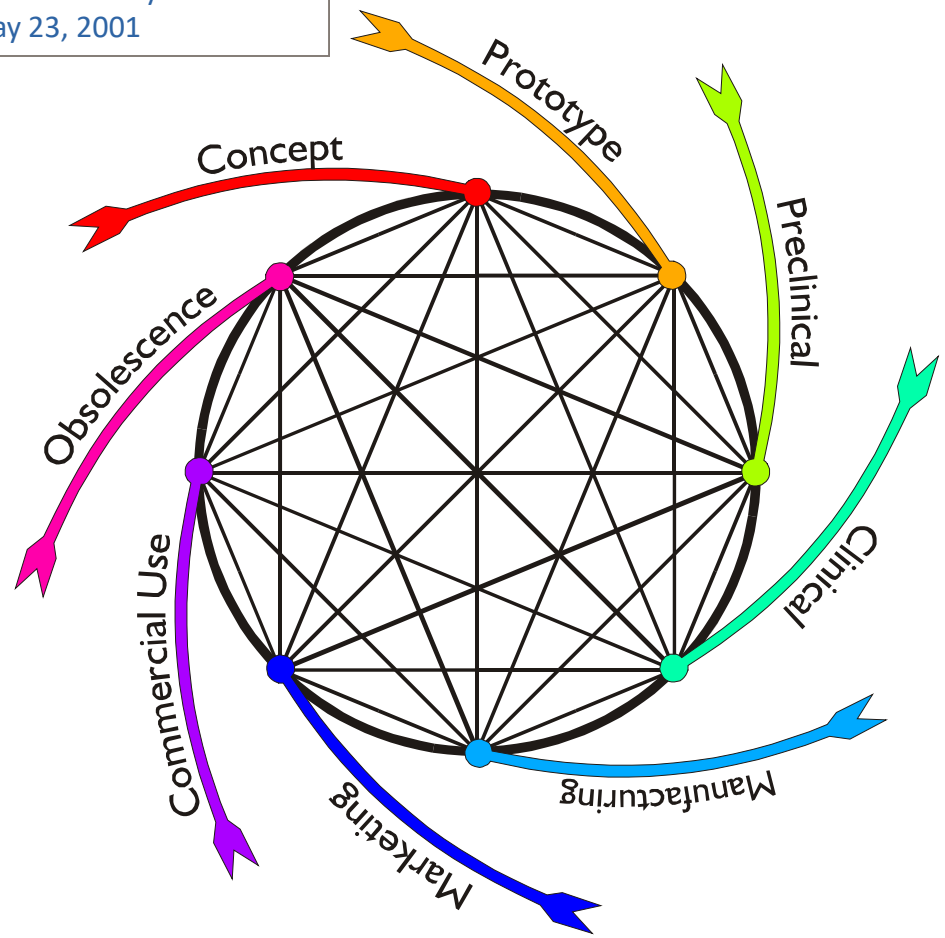
FDA Response – Early Feasibility (EF)/FIH IDE Studies

- By 6/30/2015 increase number of EF/FIH studies to each Division compared to FY 2013 performance
- Implementation:
  - Establish premarket clinical trials program in ODE
  - Incorporate benefit-risk framework
  - Establish process to resolve application-specific issues
  - Education and training for CDRH review staff
  - Develop real-time metrics to track CDRH and Industry clinical trial performance



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 Medical Devices

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.

UPI

HOME / SCIENCE NEWS

2009

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.

Cleared Devices!

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.

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.

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
- Variety of care delivery venues
- Expansionist inclusion?
- Limited information gathered
- Generalizable

Public Pressure Leads to….

Concerns (Regulatory + Public)

- Post-Marketing Surveillance (PMS) System Failures
  - Poor control over studies
    - Studies not launched
    - Poor patient enrollment
    - Poor study management
- FDA – limited authority
  - Eliminate use of withdrawn 510(k) product as predicate

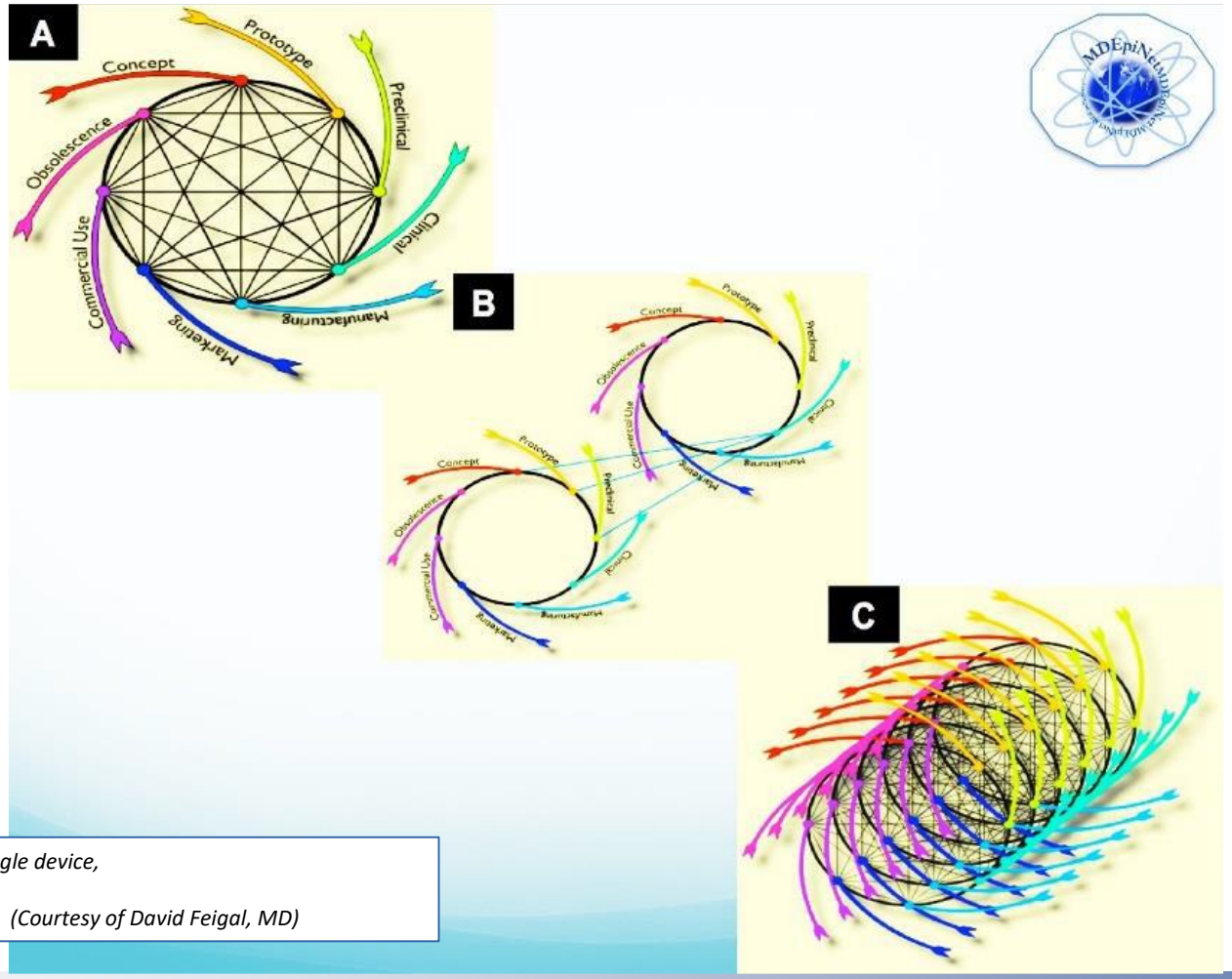
Response (Regulatory)

- Raising PMA Requirements
- Stricter PMS Reporting Requirements
- Conditional Approvals
  - Mandated PMS studies

Early Identification of Trends!

Total Product Life Cycle – from Device to Pipeline

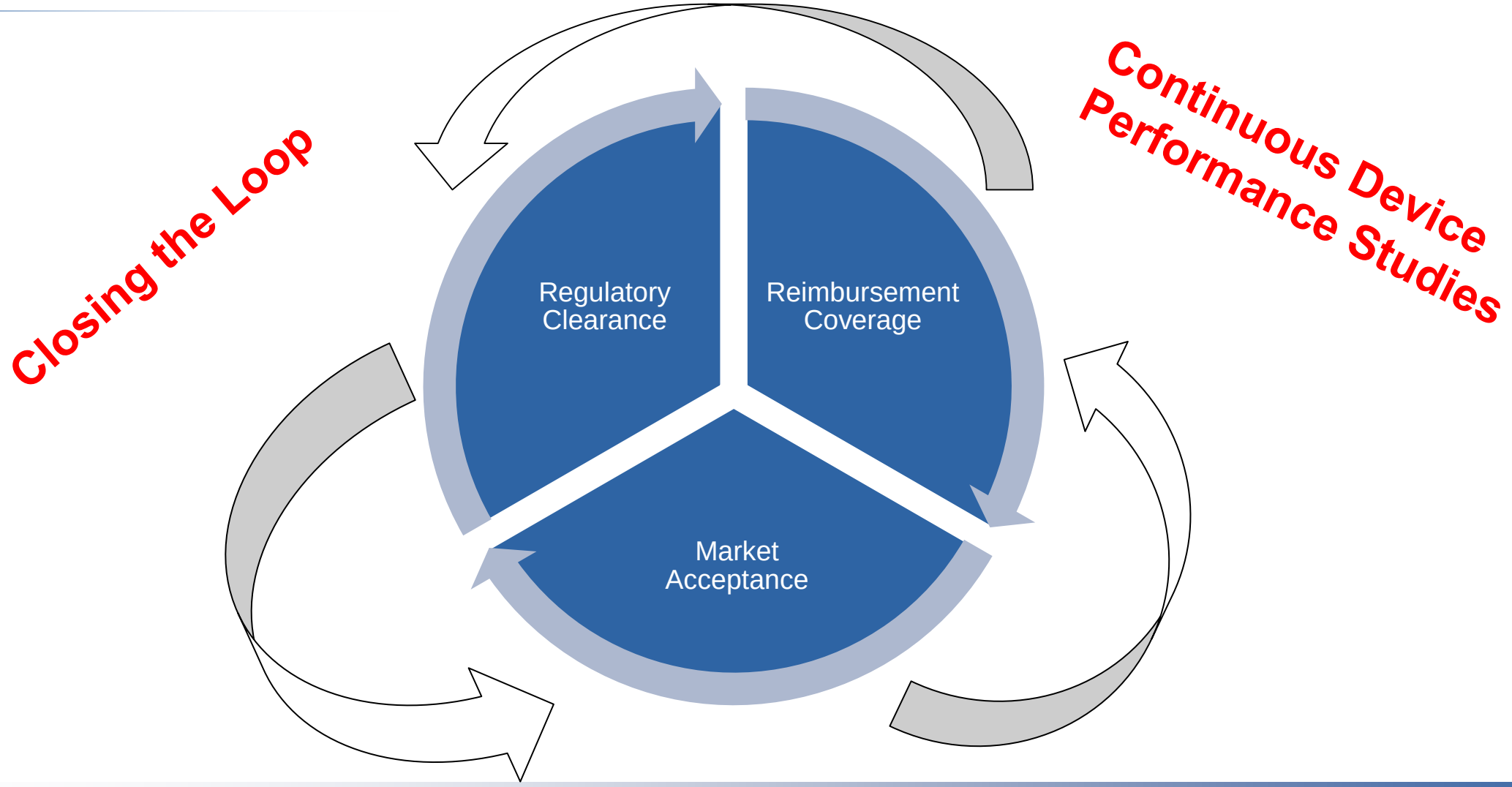
Single Device



Pipeline

Figure 2. The TPLC information accrual concept for A) a single device,
B) progression from one device design to another and
C) through the maturation of a device pipeline. *(Courtesy of David Feigal, MD)*

The New Interconnected Paradigm

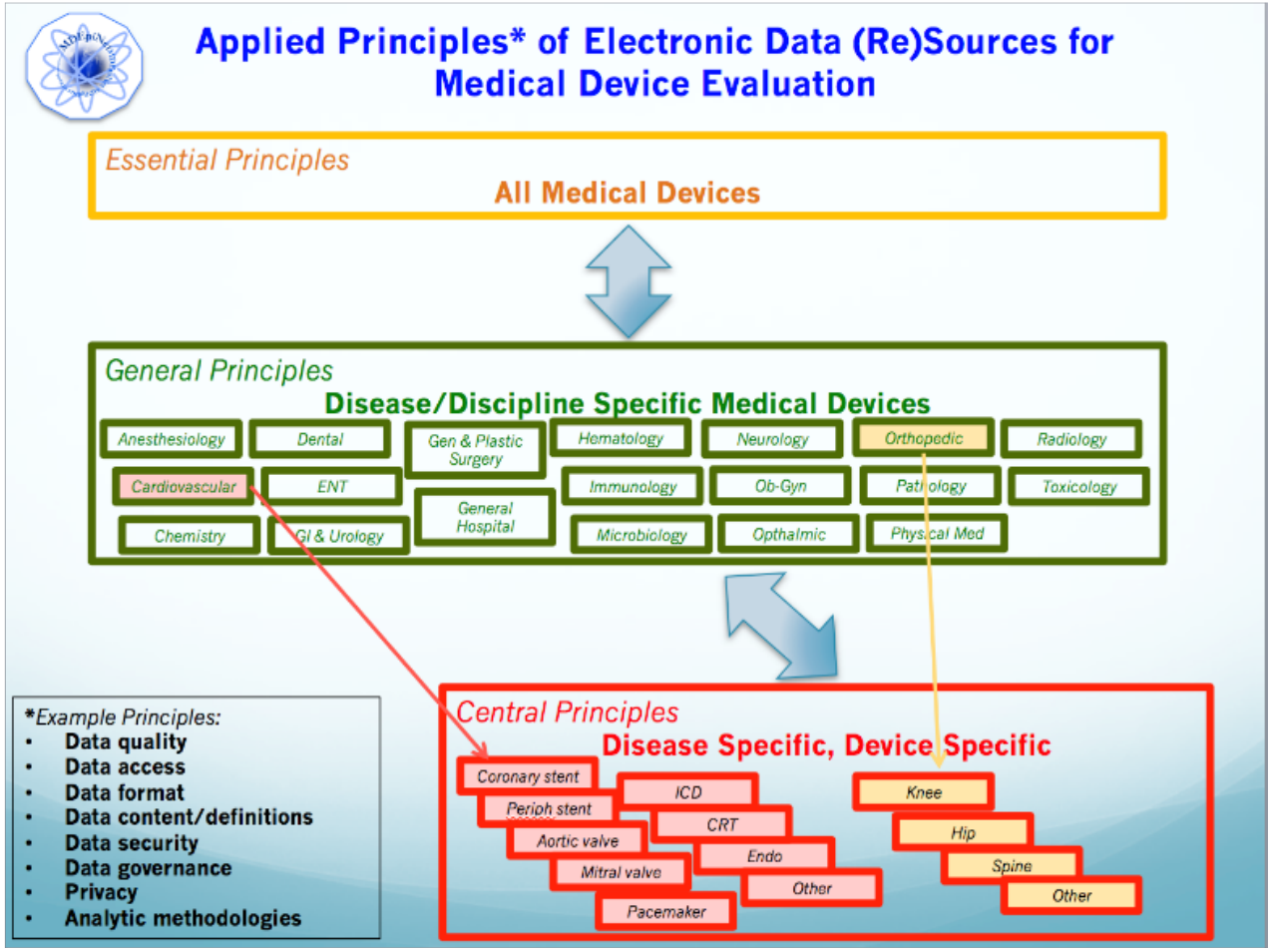


Development of National Medical Device Evaluation System

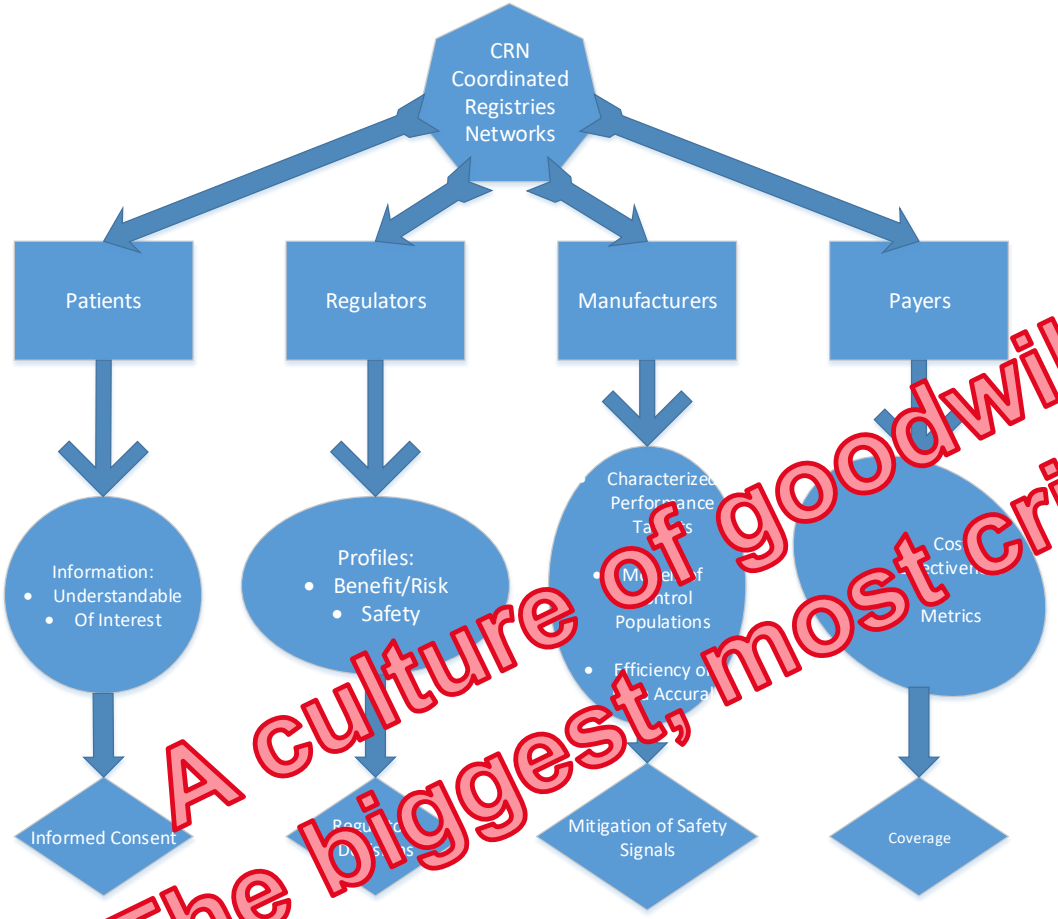
- 2012 – FDA Initiative to strengthen Device Post-market Surveillance
- 2014 – two parallel groups (MDEpiNet + MDRTF)
  - **MDEpiNet** Medical Device Epidemiology Network
  - **MDRTF** – Medical Device Registries Task Force
  - Support better regulatory decisions
  - Serve stakeholders – medical device 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)**
  - **Report – August 20, 2015**
  - Medical Device Registry Task Force & Medical Devices Epidemiology Network
- Recommendations
  - Multi-pronged approach – support different stakeholders
  - **Electronic Health Records** – key for implementation
  - Use of **UDI** (Unique Device Identifier) 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 implementation plan
  - Years 3 – 7: Implementation



New Paradigm for PMS* – National Device Evaluation System

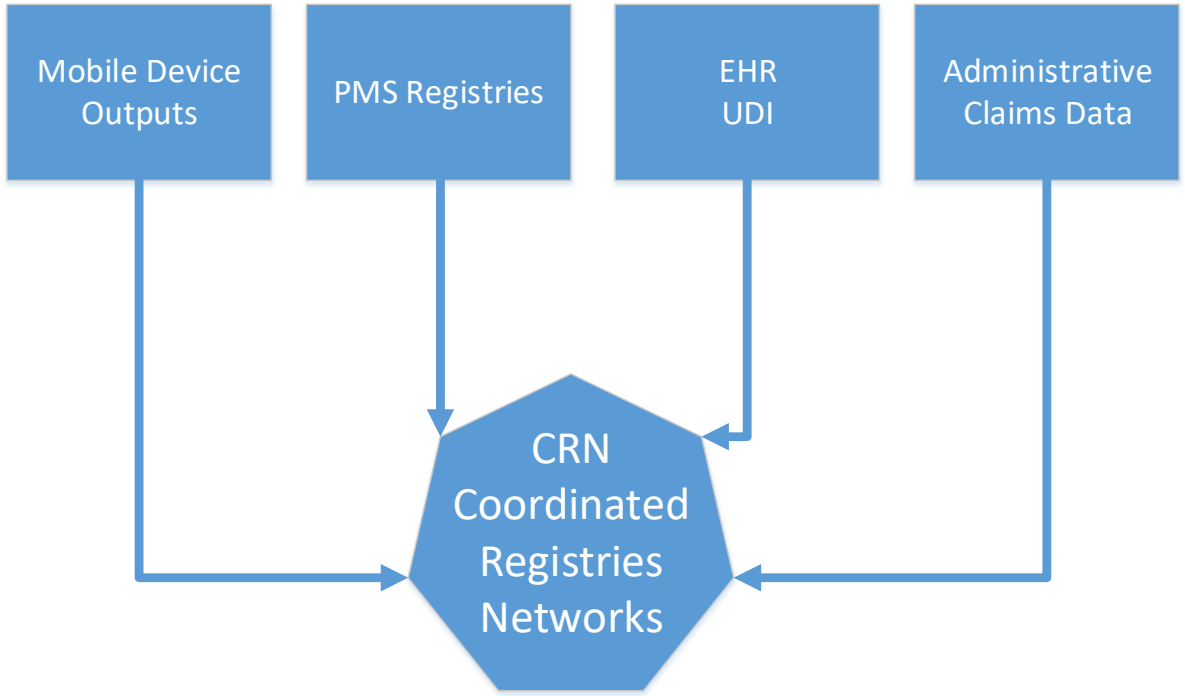


- Coordinated Registry Networks
- Ful Stakeholders
- Different
  - Interests
  - Information
  - Goals
  - Uses
- ‘Same’ information

A culture of goodwill and partnering:
The biggest, most Critical challenge of all

* 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)

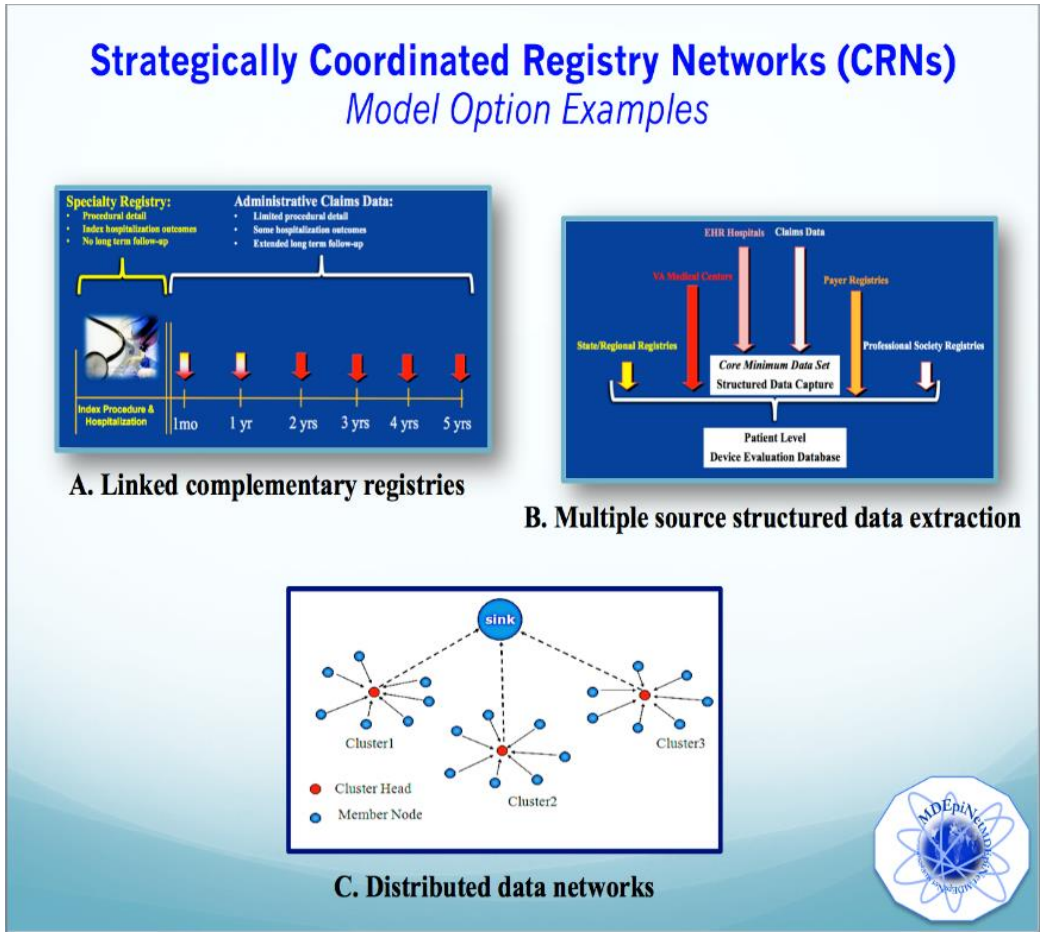
Examples of Existing Registries

- 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

Interoperability Constructs for CRNs



- (A) Complementary Registries
  - Example – TVT Registry + Administrative Registry
    - Registry #1 – Device and procedure information
    - Registry #2 – Claims / long-term follow-up information
- (B) Smart EHR Filters
- (C) ICOR – International Orthopedic Implant Safety

Figure 3. Examples of interoperability constructs for CRNs (Modified, courtesy of Matthew Brennan, MD)

Principles for Establishing CRN Functionality

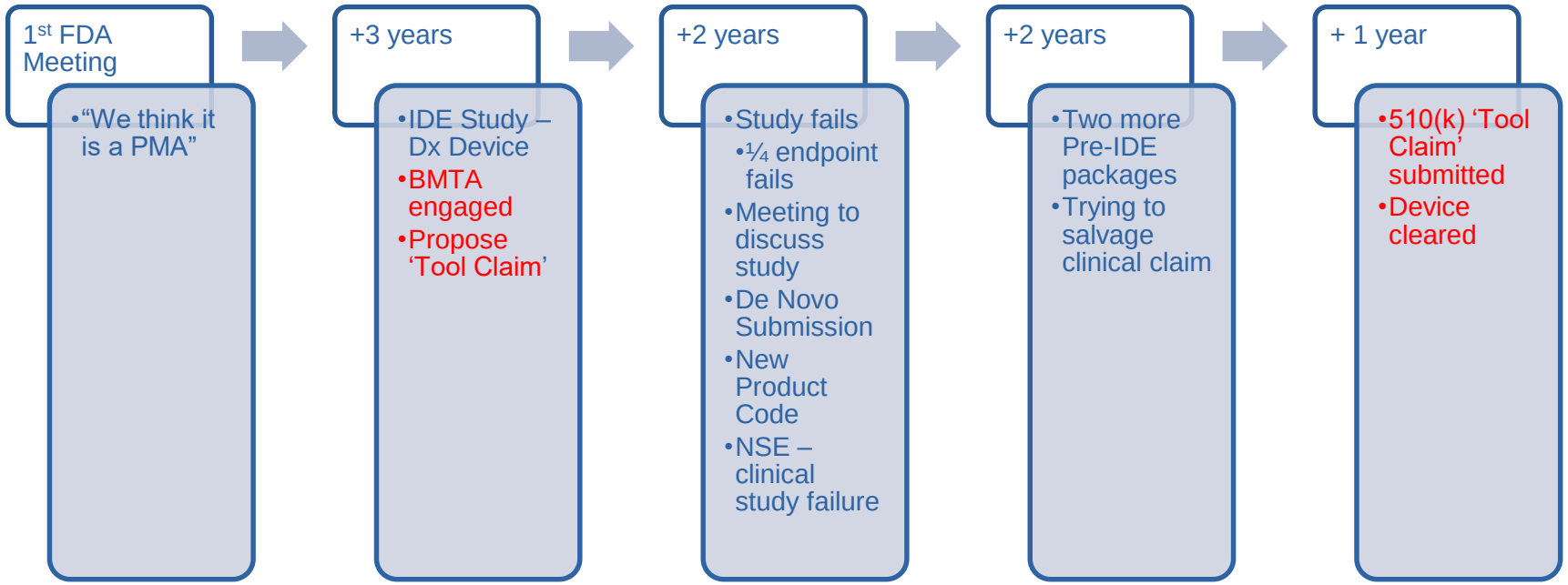
- Device identification
- Use of standardized
  - Clinical vocabulary
  - Common data elements
  - Outcome definitions
- Generalizable interoperability solutions
  - Linking disparate data sources
- Creating partnered, inclusive governance
- Develop value-based incentivized sustainability

- 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

1st and Most Important Task – Thinking Through Regulatory Approach



Exceptions do happen – Failed study sometimes leads to modified clearance

Thank You!

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