The State of CDRH and Future Directions

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U.S. Food and Drug Administration

Patients are at the Heart of What We Do

CDRH Vision

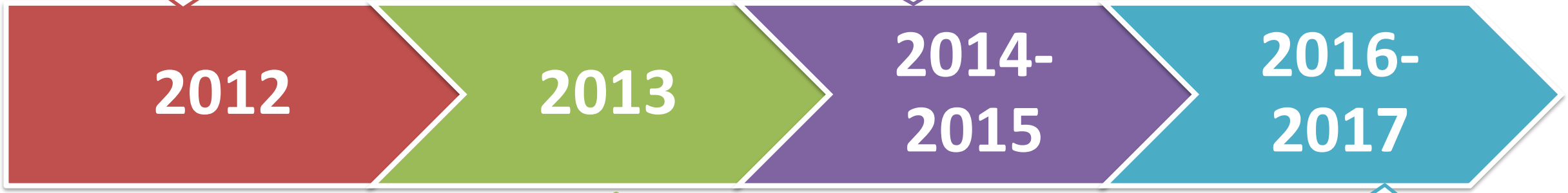
Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world

Vision, Mission, and Shared Values

"Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world…."

Clinical Trials, Premarket/Postmarket Balance, & Customer Service

A different approach—holding ourselves accountable for achieving measurable outcomes in specific areas.



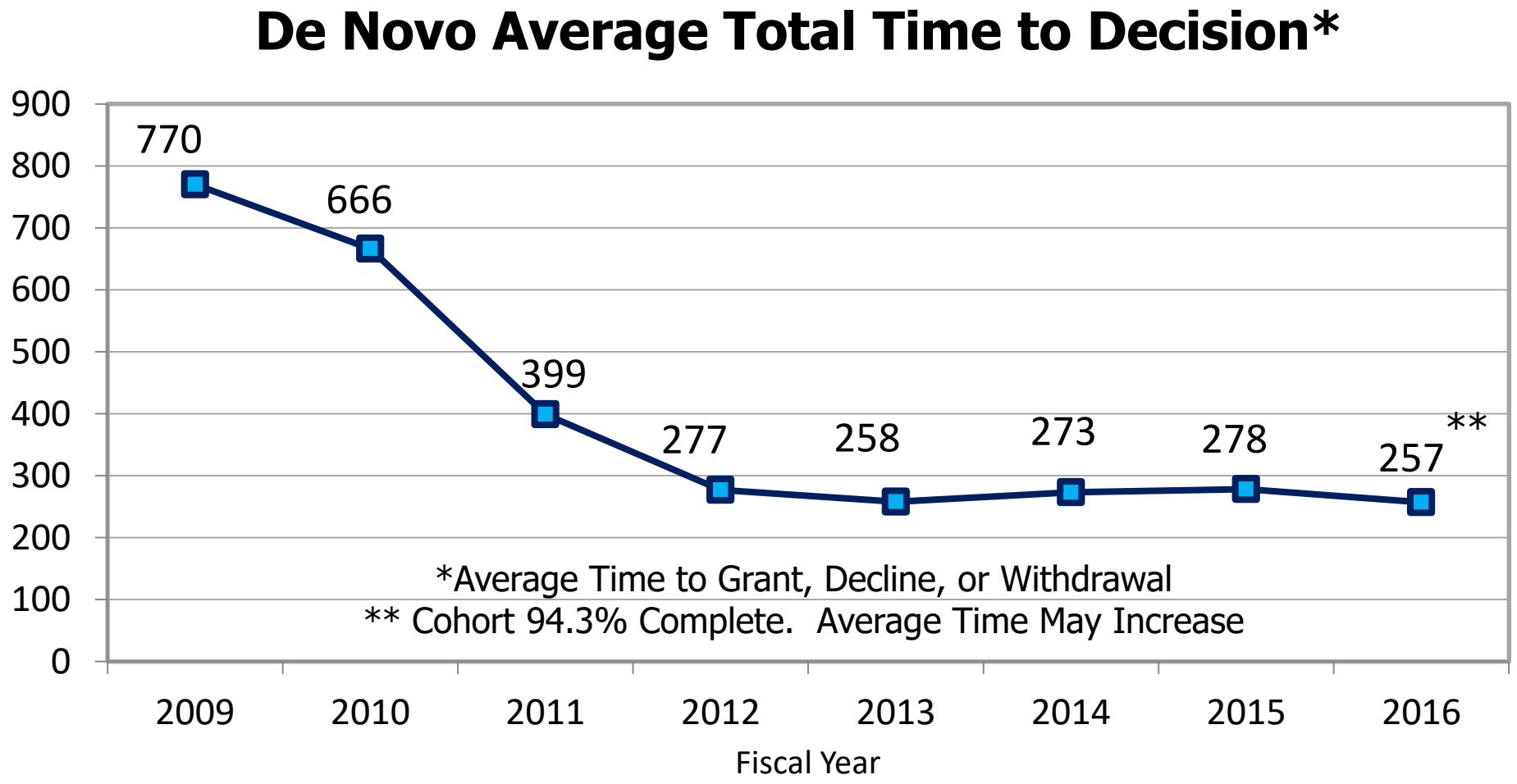
Re-aligned our Strategic Priorities to support the achievement of our Vision **MDIC, IMDRF, Entrepreneurs in Residence…**

NEST, Partner with Patients, & Culture of Quality

Building on success.

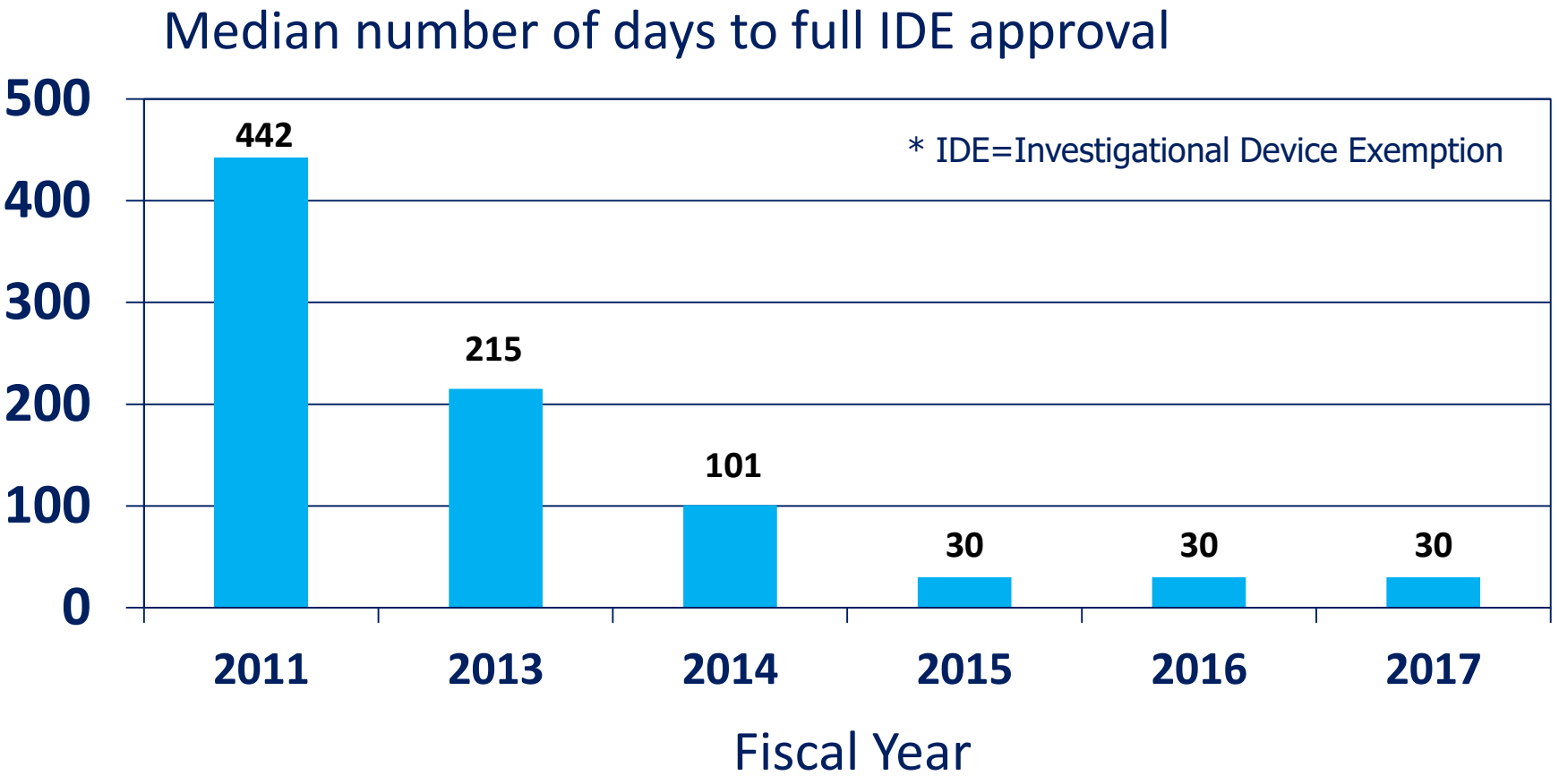
Moderate Risk Innovative Devices (De Novo)

67% REDUCTION in Total Time to Decision



Clinical Trials (IDEs)*

>90% Reduction in Time to IDE Approval



Importance of Early Feasibility Studies

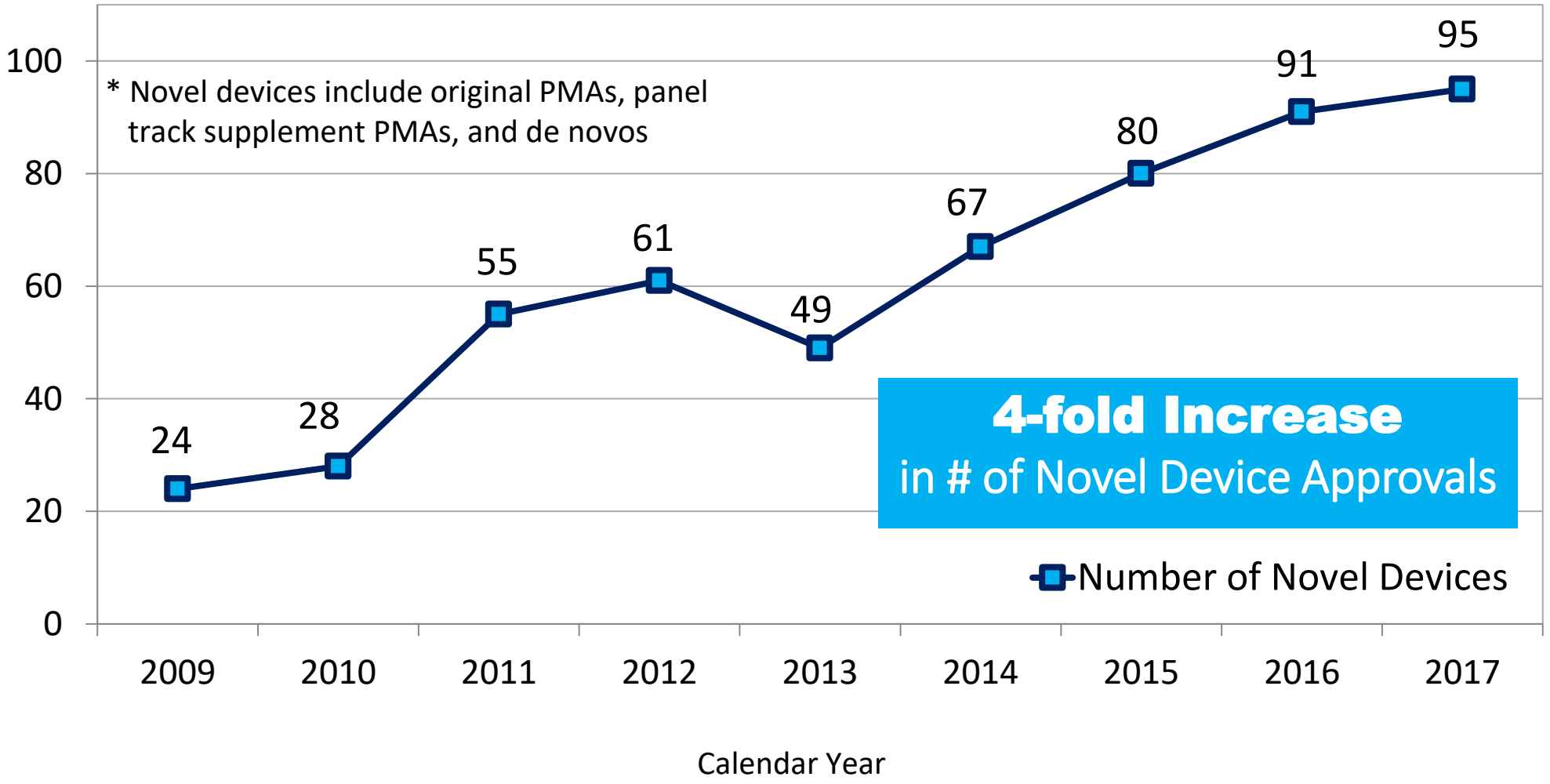
- Earliest patient access
- Close collaboration between developers & users
- Clinical study continuity from early clinical use to post-approval
- U.S. leadership and contributor to medical device innovation

U.S. Sites Re-engaging in Early Clinical Research

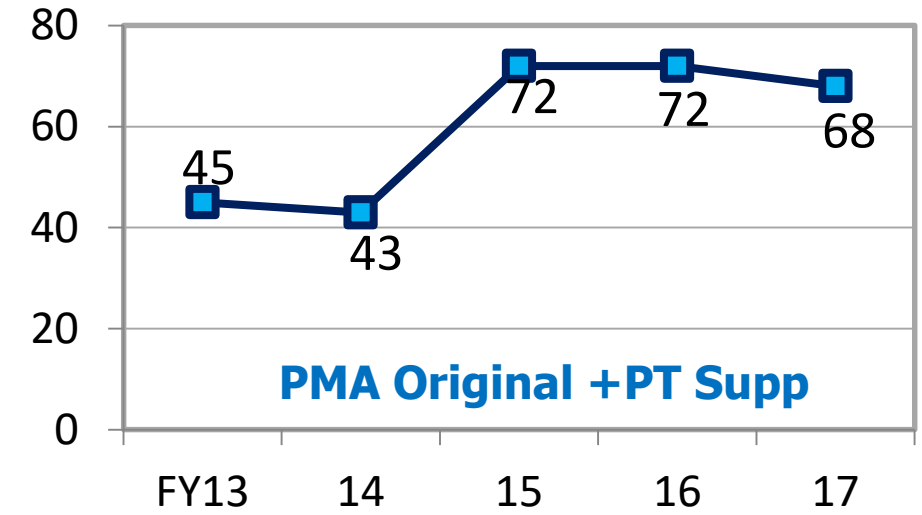
FDA Early Feasibility Study Program
2015-2017

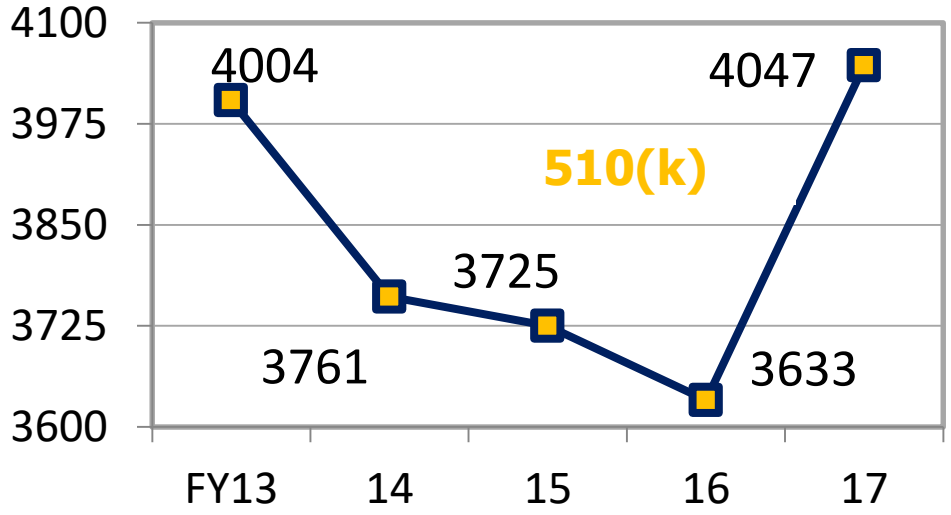
>50 Company Participants
>120 Early Feasibility IDEs
~50% Increase in Annual # of EFS IDEs

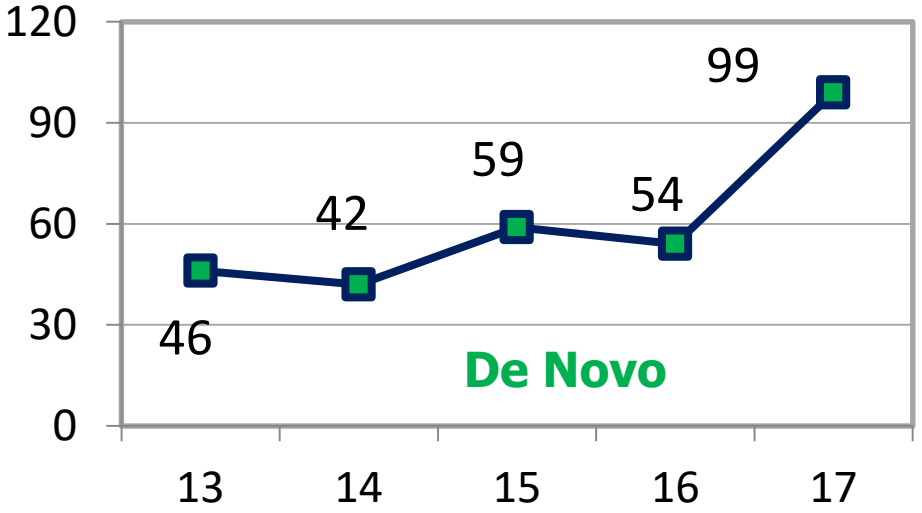
Novel Device Approvals

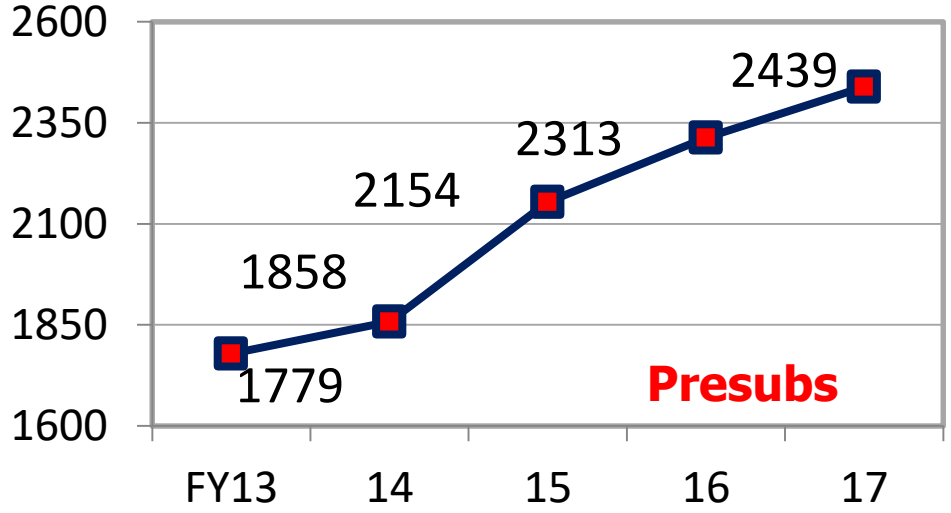


MDUFA III Submission Volume









21st Century Cures Implementation

- Establish Breakthrough Device Pathway
- Change HDE Limit to 8000 Patients
- Streamline Process for 510(k) Exemptions
- Modifications to Classification Panels
- Allow for Central IRBs
- Update CLIA Waiver Guidance
- Recognition of Standards
- Train and Audit Least Burdensome
- Clarify Medical Software Regulation
- Cleaning and Validation Data

21ST CENTURY CURES ACT IMPLEMENTATION

Provision	Implementation activities completed	Date completed
Least Burdensome	Issued draft guidance (not mandated); trained staff	15 Dec 2017
CLIA Waiver	Issued draft guidance	29 Nov 2017
Breakthrough Devices	Issued draft guidance	25 Oct 2017
Classification Panels	Published FR Notice soliciting public input for panel membership; finalized "Procedures for Meetings of the Medical Devices Advisory Committee" guidance including Cures-related changes	23 Jun 2017 (FR notice) 1 Sep 2017 (guidance)
Cleaning & Validation	Published FR Notice identifying reusable device types for which 510(k)s are required to include certain validation instructions for use and validation data regarding cleaning, disinfection, and sterilization	9 Jun 2017
Central IRB	Published amendment to regulations removing the word "local" where needed to comply with new law	7 Jun 2017
Humanitarian Device Exemptions	Amended regulations changing the HDE population limit from 4,000 to 8,000	7 Jun 2017
Exemptions	Published lists of Class I and Class II devices exempt from requirement to submit a 510(k)	Final Class I list: 13 Apr 2017 Final Class II list: 11 Jul 2017
Software	Detailed on subsequent slides	

Breakthrough Device Pathway (Formerly Expedited Access Pathway)

Breakthrough Devices Program

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on October 25, 2017.

65 devices accepted into the program since April 2015

1st breakthrough device approved December 2017

- Interactive & Timely Communication
- Pre-Postmarket Balance
- Flexible Clinical Study Design
- Senior Management Engagement
- Priority Review

MDUFA 4 Implementation

- **Add Performance Goals for Presubmissions and De Novo**
- **Reduce 510(k) Total Time to Decision**
- **PMA Approvable and Post-Panel Decisions**
- **Improve Deficiency Letter Writing**
- **Enhance Use of Consensus Standards**
- **Establish Digital Health and Quality Management Programs**
- **Independent Assessment/Auditing**
- **Patient Engagement**
- **Real World Evidence**

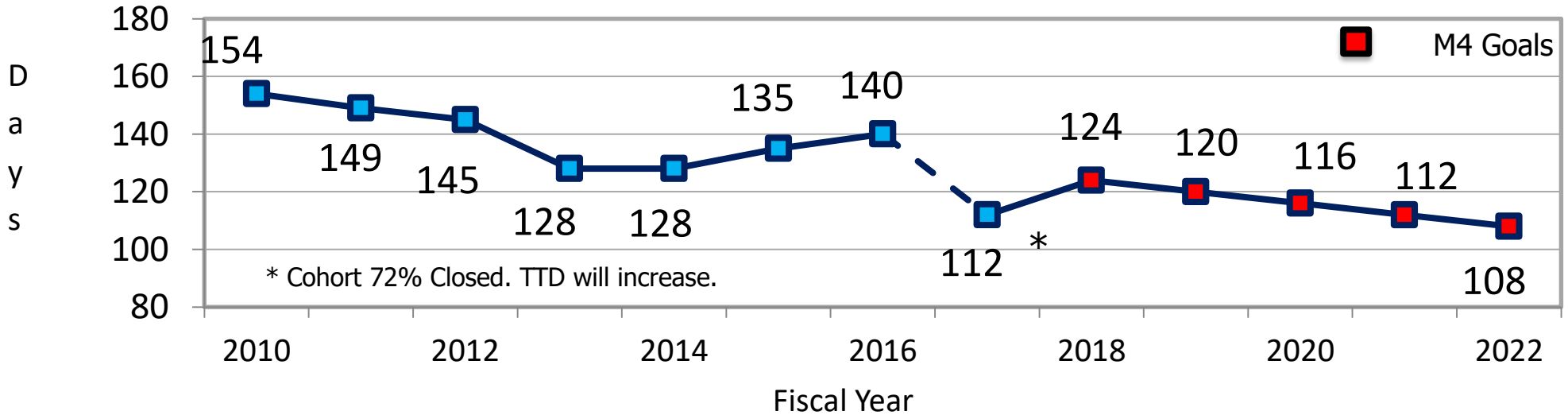
Launch Date: October 1, 2017

MDUFA 4 Implementation

- Request for comments on Voluntary Malfunction Summary Reporting Program (26 Dec 2017)
- Accessories guidance (20 Dec 2017): to implement new review timelines and process for accessories
- Pre-Sub guidance (29 Sep 2017): to update timelines related to scheduling meetings and FDA feedback
- Deficiencies guidance (29 Sep 2017): to clarify that a deficiency should include a reference to a regulation, final guidance, or standard

510(k) Total Time to MDUFA Decision

Target: 23% REDUCTION in Total Time to Decision



Strategies for Reducing TTD

- RTA Addendum
- Day-10 Call
- Branch Level SE
- Increased Use of Special 510(k)
- Increase Use of Proceed Interactively
- Clarify Policies for Common Deficiencies

RTA

- **Inclusion of RTA Addendum with RTA Decision:** Used to provide early notification to sponsors of "observations" made during initial RTA review, that if addressed, would streamline submission review.

Substantive Review

- **Quick Review –** Submission triage prioritizing review of high quality, straightforward submissions with goal of completing these submissions interactively, without a hold.
- **Update PI Policy –** Set target PI rates, clarify expected sponsor response timelines and establish interactive approach to PI decision.

Hold

- **10-day Call –** Introduce voluntary 10-day call following issuance of AI or MAJ letter to ensure sponsor understands deficiencies.
- **Use SIM to assess justifications in lieu of providing data –** If submitter chooses to provide a justification in lieu of testing, submitter can address justification via a submission issue Q-Sub to ensure AI response contains all necessary data.
- **Flag –** Following 10-day call, submitter can request senior management/expert review of decision on deficiencies of greatest concern to the submitter.

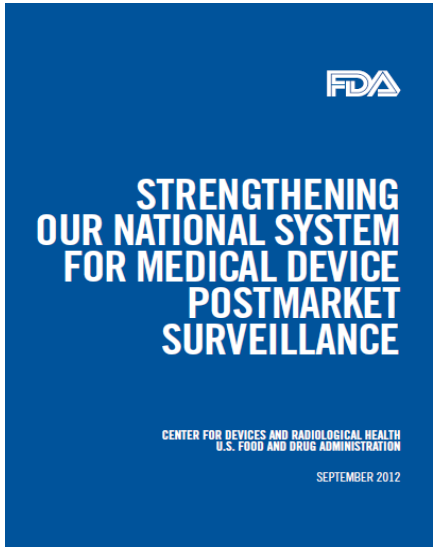
Interactive Review

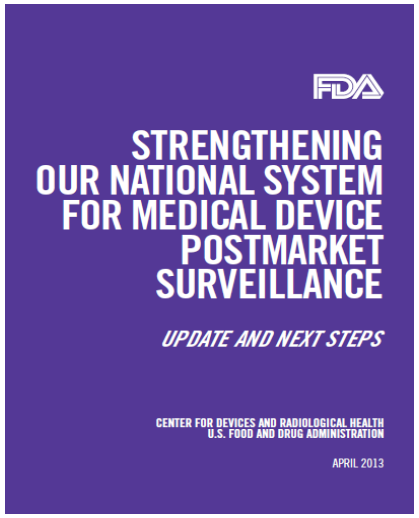
- **Clarify "two ask" policy:** Promote earlier interactive communication of identified submission issues.

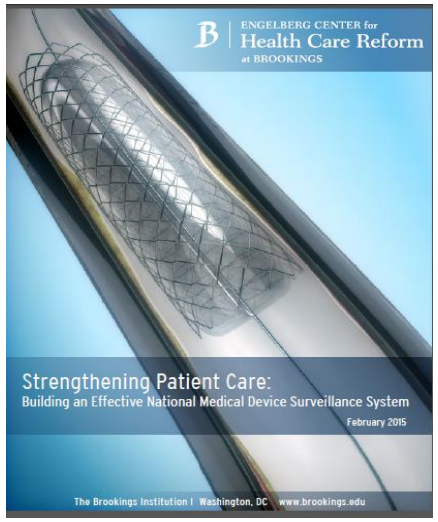
Decision

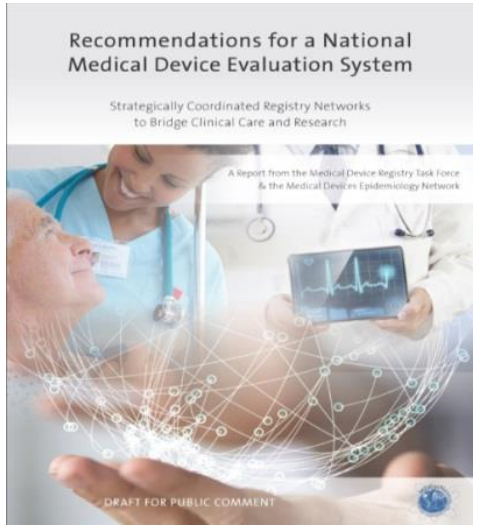
- **First round NSE -** A submission does not have to go on hold before certain NSE recommendations can be issued (e.g. new intended use, no valid predicate) as long as the submitter had an opportunity via interactive review.
- **Branch-level SE concurrence -** Straight forward SE letters can be signed out at the branch level instead of the Division level. This approach reduces time spent waiting for Division review and concurrence.

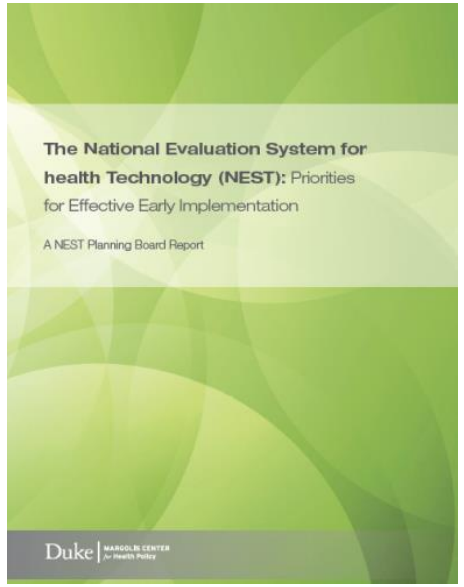
Foundational Work on NEST





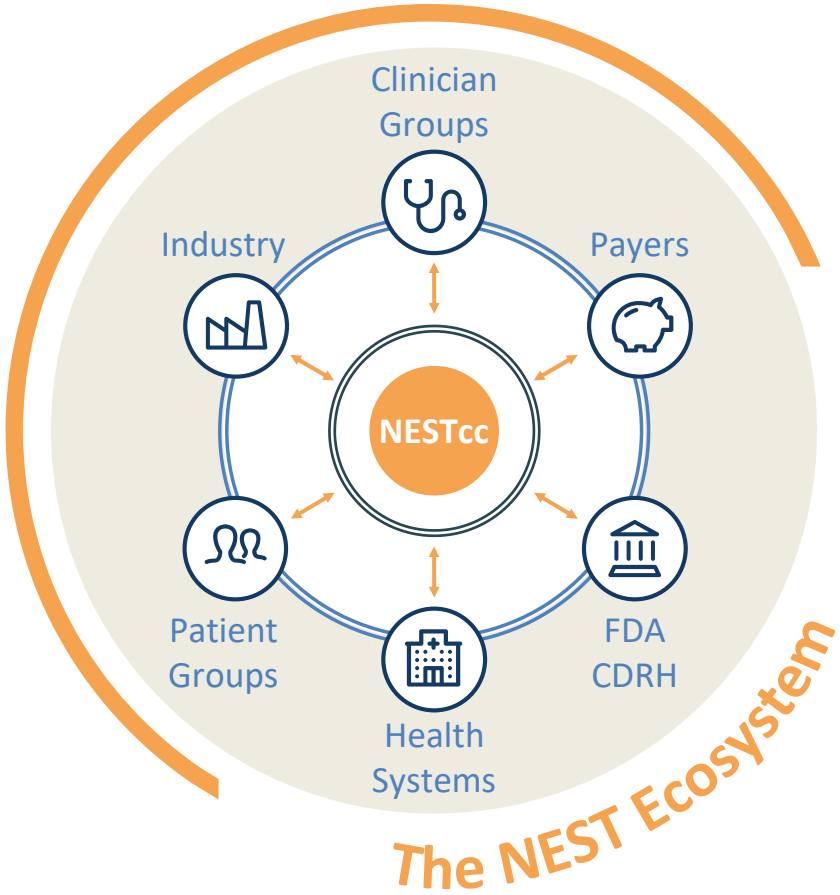






NESTcc should serve as a catalyst to support the timely and reliable development of high-quality RWE

- Establish **partnerships** with a range of organizations, companies, and collaborations that provide data and analytics solutions
- Set **data quality standards** for data partners and **methods standards** for observational and randomized studies
- Offer **value** through products and services to key stakeholders in the ecosystem



DEVELOP NESTcc'S ROLE: BUILDING A DATA NETWORK

NESTcc surveyed its Data Network to determine current capabilities, gaps, and priority areas

Engage

Leverage

Transform

NESTcc Network Collaborators Surveyed

Duke University Health System • HealthCore • Lahey Clinic • Mayo Clinic • MDEpiNet • Mercy • OneFlorida • PEDSnet • Vanderbilt University • Weill-Cornell Medical Center • Yale New Haven Health System

Survey respondents represent:

150 Hospitals

3,042+ Outpatient Clinics

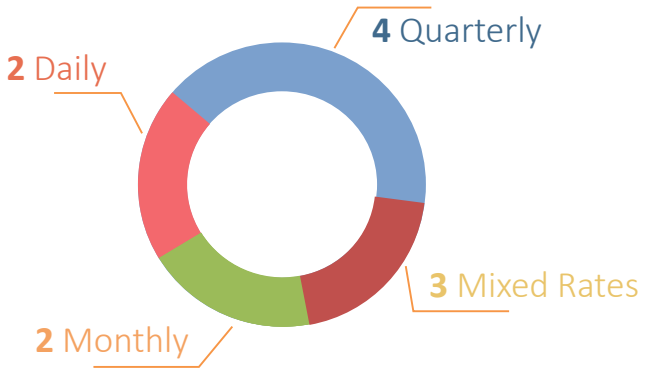
Patient data represents:

469M+ Patient Records

Common data models:

- ✓ I2b2
- ✓ OMOP
- ✓ PCORnet
- ✓ Sentinel

Respondents report regular data refreshes:



Most cited expertise:

- ✓ Cardiovascular and Cardiac Surgery
- ✓ Women's Health
- ✓ Neurosurgery
- ✓ Gastroenterology
- ✓ Orthopedic

DEVELOP NESTcc'S ROLE

NESTcc's value proposition will be established through use cases that span the Total Product Life Cycle (TPLC) and include interventional and observational study designs

PRIORITY USE CASES

Pre-Market: PMA, 510(k), De Novo

Using RWE to inform pre-market development or incremental improvement of medical devices

Label Expansion

Using RWE in a regulatory submission to support an expanded indication for use of medical devices already on the market

Post-Market Approval Studies (PAS)

Using generated RWE to track medical device's safety and effectiveness as part of its condition of approval

Surveillance

Using generated RWE to track and document medical device safety and effectiveness for products on the market

Coverage

Using generated RWE to support coverage and reimbursement decisions by public and private payers

FDA-CMS Parallel Review

Exact Sciences

Cologuard – Colon cancer screening

Foundation Medicine

FoundationOne – genomic profiling companion diagnostic

FDA approval & CMS proposed NCD on Same Day

Opportunities To Obtain Payer and Health Technology Assessment Input

- Public Payer Presubmission Participation
- Opportunity to Obtain Private Payer Input

Current Participants:

- BlueCross BlueShield Association
- Duke Evidence Synthesis Group
- ECRI Institute
- Humana
- Kaiser Permanente
- National Institute for Health and Care Excellence
- United Health Group

- ❑ Voluntary Program
- ❑ Obtain input on clinical trial design or other plans for gathering clinical evidence

For more information: Google Search “CDRH Payer Program”

CDRH Strategic Priorities 2018-2020

Making Our Vision A Reality

The Strategic Priorities will focus on the enhancement and widespread application of three approaches we've already started

Employee Engagement, Opportunity, and Success

Simplicity

Collaborative Communities

Our Measure of Success

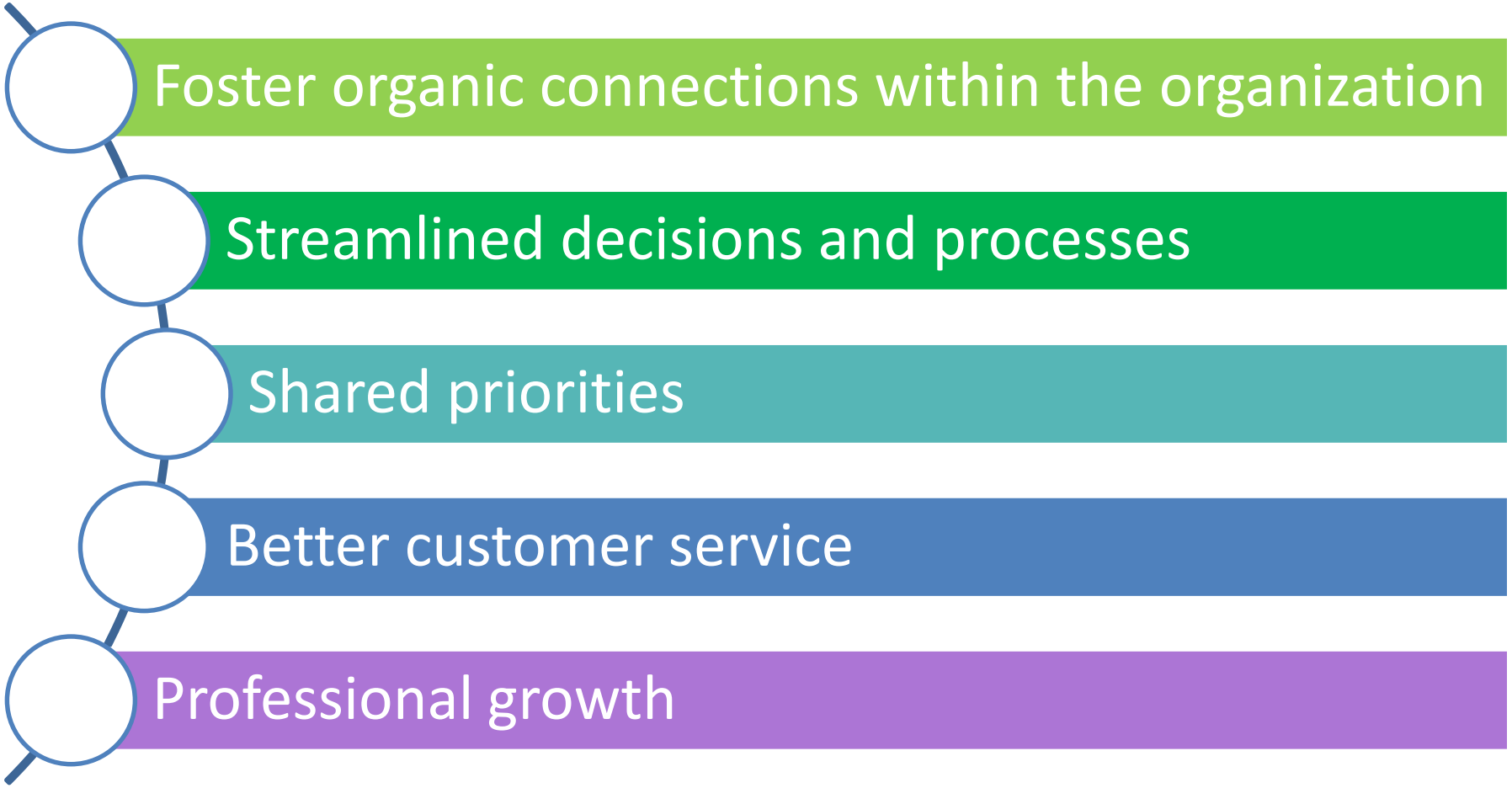
By December 31, 2020, more than 50 percent of manufacturers of novel technologies for the U.S. market intend to bring their devices to the U.S. first or in parallel with other major markets.

2018-2020 Strategic Priorities

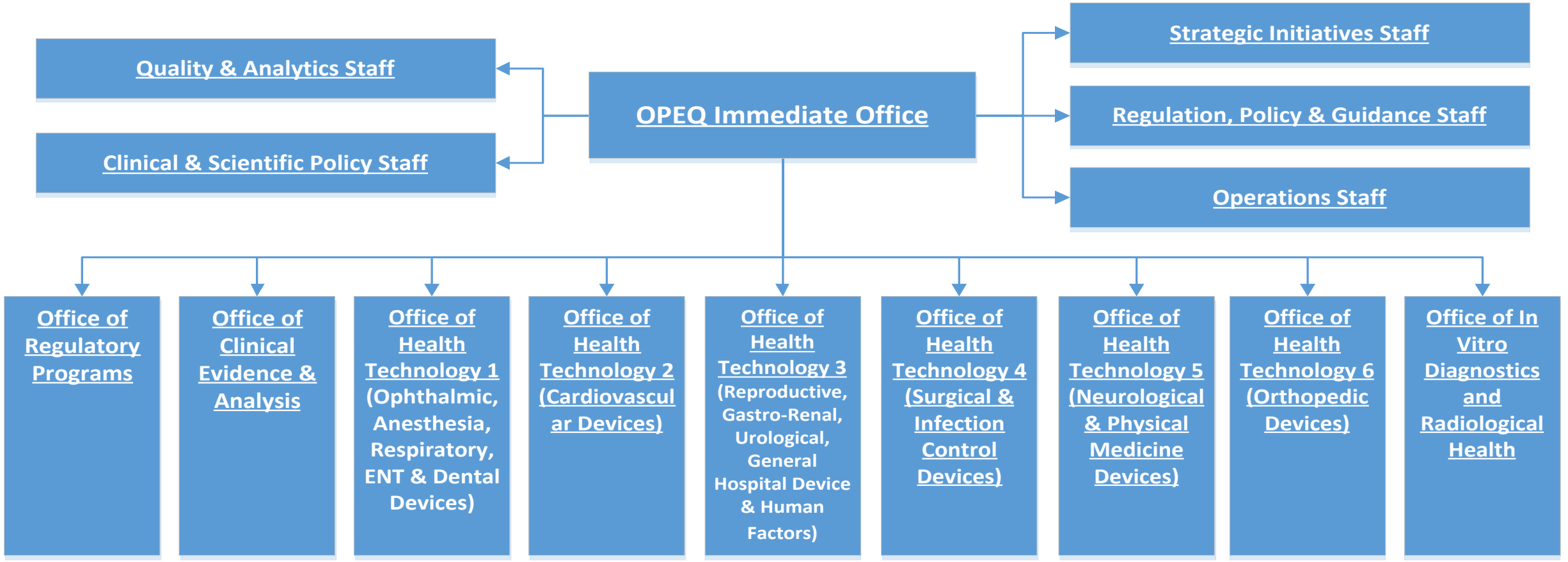
Employee Engagement, Opportunity, and Success

- Reduce unnecessary burdens
- Foster creativity and teamwork
- Facilitate open dialogue
- Promote an environment of trust and mutual respect
- Create opportunities for professional growth and personal development
- Provide a reasonable work life balance

Total Product Lifecycle (TPLC) Reorganization



Office of Product Evaluation and Quality (OPEQ) Structure



2018-2020 Strategic Priorities

Simplicity

- Streamline our policies, processes, programs, and approaches, as appropriate
- Stop doing or streamline what we determine is not sufficiently “value added”
- Remove unnecessary burdens (both on our customers and ourselves)
- Continuous process improvement
- Develop policies that are straightforward
- Spend more time on what matters most

2018-2020 Strategic Priorities

Collaborative Communities

- Forum where public and private sector members work together on an ongoing basis to achieve shared outcomes and solve both shared problems and problems unique to other members
- In an environment of trust and openness, where participants feel safe and respected to communicate their concerns
- Where members share a *collective responsibility* to help each other obtain what they need to be successful
- And government has a seat at the table but does not run the forum

What's Ahead for 2018 and Beyond?

Voluntary Medical Device Manufacturing and Product Quality Pilot

Pilot program

- 3rd-party maturity appraisal that leverages the Capability Maturity Model Integration (CMMI) framework to assess a medical device organization's capability to produce high-quality devices and increase patient safety
- Pilot was announced on December 28, 2017 and will run from January 2, 2018 and continue through December 28, 2018

FDA adjustments

- Forgo surveillance, appropriate post-approval, and risk-based inspections
- Manufacturing change notice submissions
  - Streamlined submission
  - Accelerated acceptance 2 business days vs. 30 days
- Manufacturing site changes
  - Streamlined submission
  - Accelerated approval – 1 week target
- Original PMA manufacturing section
  - Streamlined submission
  - Forgo preapproval inspection

These changes reduce the burden and disruption of audits, accelerate the review and approval process for changes, and shift resources to innovation and improvement

How are Manufacturers Perceiving the Difference in the 2 Processes?

	FDA inspection	CMMI appraisal
Mind-sets	• Only answer questions asked	• Be open in answering questions • Weaknesses are opportunities to improve business processes
Discussion	• Do not discuss improvement opportunities or future plans	• Talk about improvements made over time and where we are going
Interaction	• Inspectors interrogate quality leaders, process experts, and record owners • Inspectors look for evidence of noncompliance to regulations	• Appraisers conduct group interviews of “doers” responsible for work products • Appraisers engage in discussions to truly understand how the business operates relative to best practices
Time investment	• Large support team with backroom/ front room, streams, scribes, etc. • **2-day inspection, 1,370 hours**	• Minimal disruption to site resources and no need for backroom/front room • **5-day appraisal, 340 hours**

Expanded Abbreviated 510(k)

- Moderate risk devices are evaluated through 510(k) Program
- Require demonstration of "substantial equivalence" to a predicate device
- Direct comparison to a predicate device may be burdensome and unnecessary
- Abbreviated 510(k) submission program relies on guidance documents, special controls, and FDA-recognized consensus standards to facilitate 510(k) review

CDRH Proposed Expansion of the Abbreviated 510(k) Program

- Optional approach for certain, well-understood device types
- Demonstrate new device meets FDA-identified performance criteria
- Transparency about device performance for health care providers and patients
- Introduces opportunities for international harmonization

Appropriate Level of Uncertainty

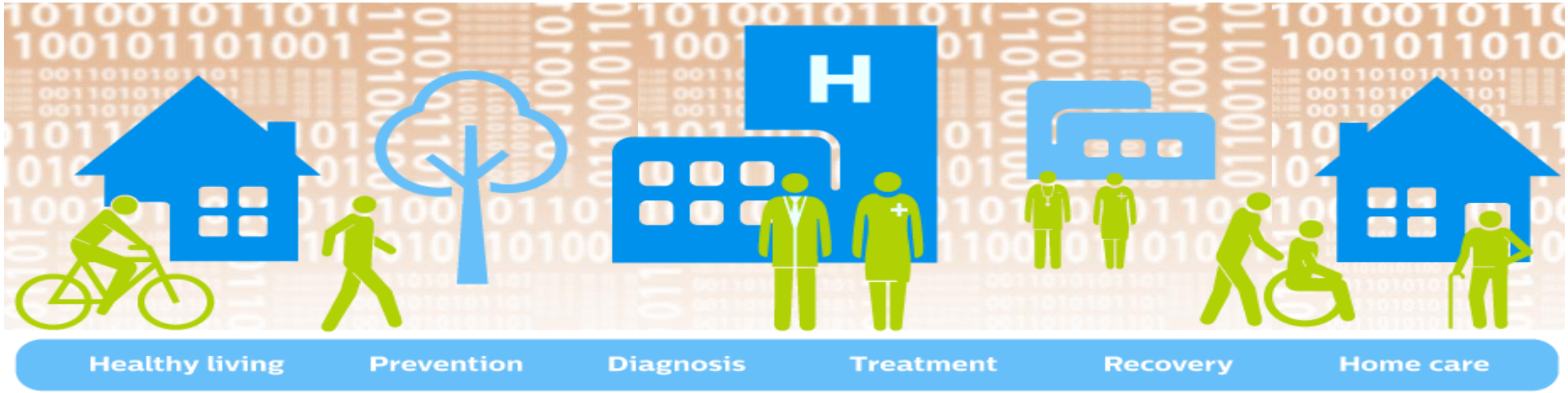
- Some degree of uncertainty generally exists around benefits and risks for regulatory decisions
- The regulatory standard is reasonable assurance – not absolute assurance
- Flexible regulatory paradigm

CDRH Intends to Clarify Through Guidance
Circumstances Where FDA is More Likely to Accept More Uncertainty

For example:

- Breakthrough Devices
- PMAs with small patient population
- De Novos with minimal risk
- Particularly if established postmarket data collection mechanism

Digitization Across the Health Care Continuum



Moving health care from the Clinic to the Patient

Understanding patient's behavior and physiology "*In the wild*"

Focusing on prevention for early/smaller interventions

Leveraging **computing power, sensors, connectivity** ***and*** **software**

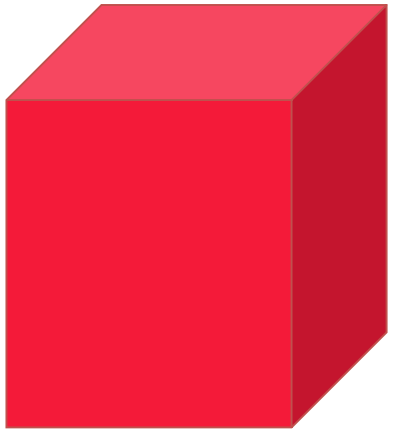
Current Regulatory Paradigm Not Well-Suited

Current Regulatory Paradigm

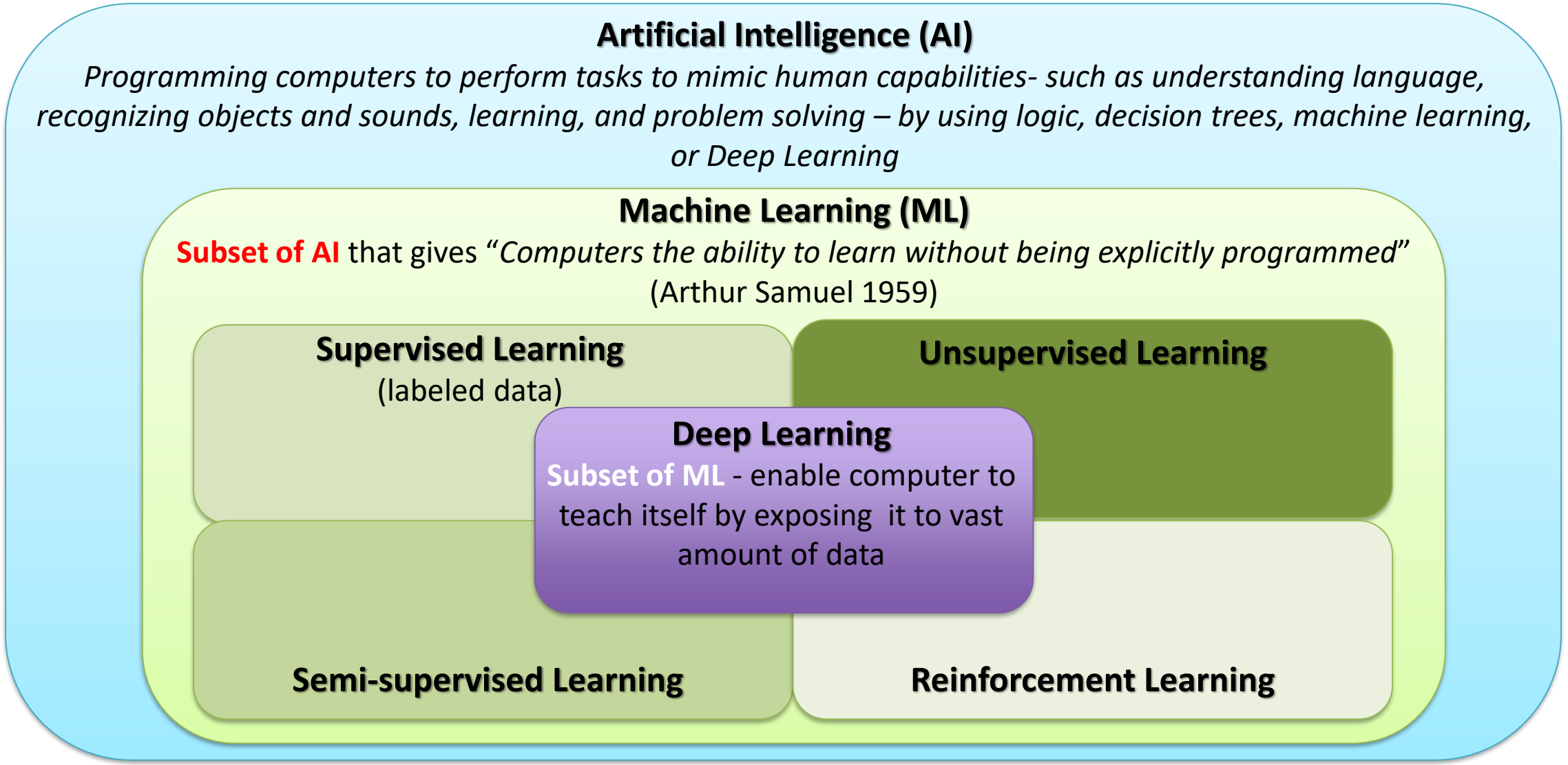
- Premarket timeline suited for hardware based products
- Deterministic risks and benefits, distinct responsibilities, physical products
- Program capacity manages – 3,500 510(k) submissions / 2400 pre-submissions

Unique Aspects of Digital Health

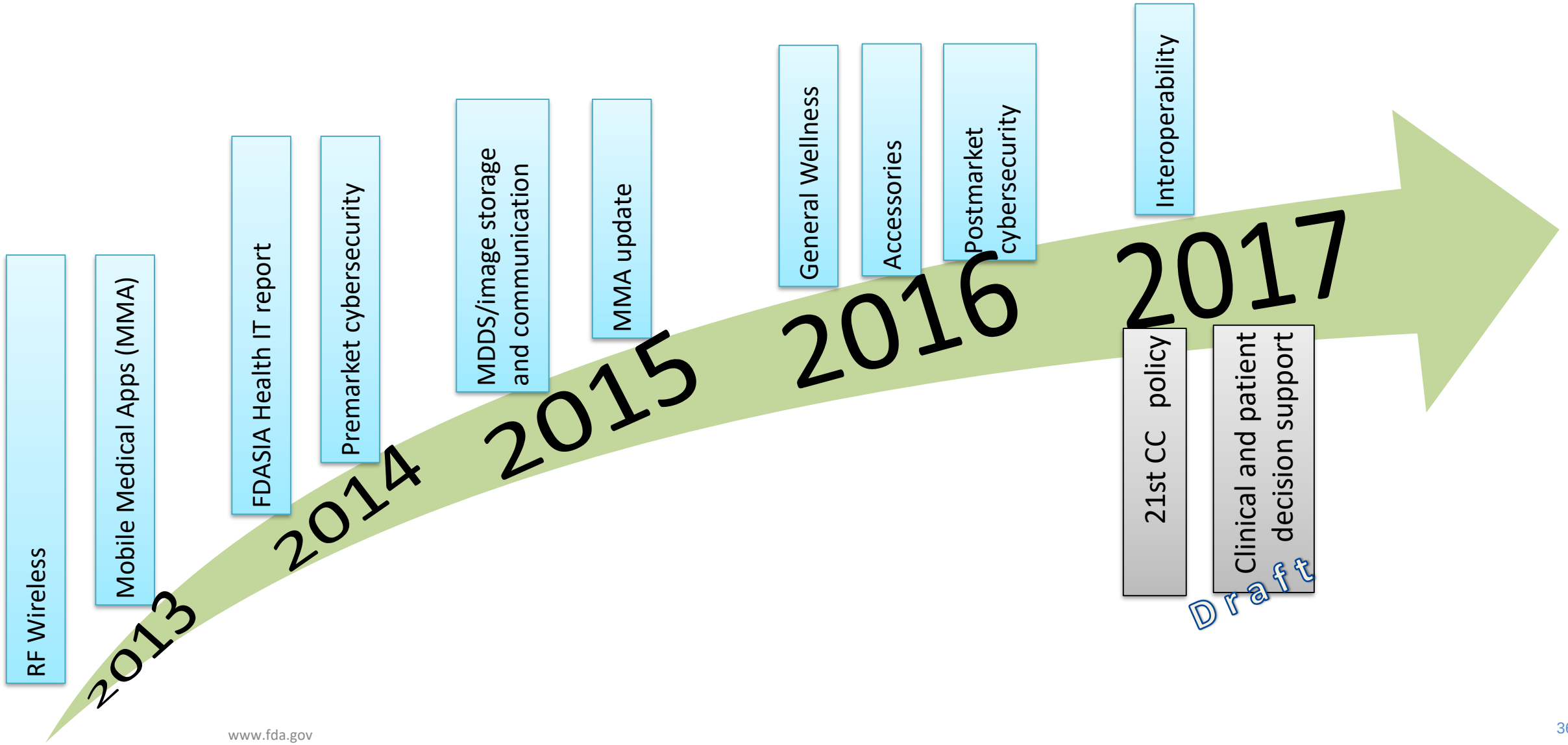
- Software development timelines + software development practices + rapid iterations
- Emerging issues – (cybersecurity; shared responsibilities, non-physical products)
- Potential for exponential increase in volume of submissions



World of SaMD and Artificial Intelligence

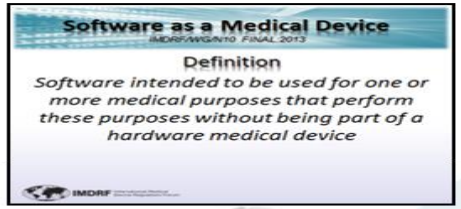


Balancing Innovation and Patient Safety with Foundational Policies

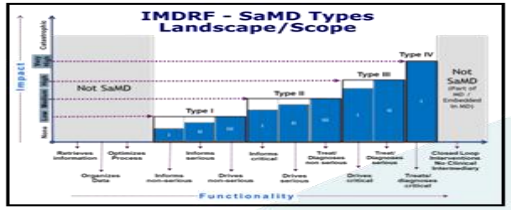


Leading International Convergence effort on Software as a Medical Device (SaMD)

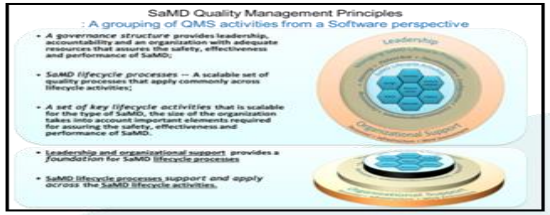
International Medical device Regulators Forum (IMDRF):
A converged SaMD framework and associated controls.



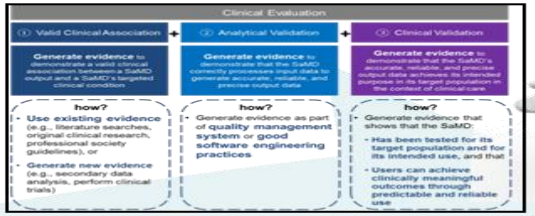
2013
Foundational vocabulary



2014 – Risk framework based on impact to patients



2015 – Quality Management Systems (QMS) control ➔Translating Software development practices to regulatory QMS



SaMD – Clinical Evaluation ➔Generating evidence for clinically meaningful SaMD

21st Century Cures Act – Codifies FDA Policies

Amended the definition of "device" in the Food, Drug, and Cosmetic Act to exclude certain software functions intended...

FDA policies affected/codified

(A) *for administrative support*

FDASIA Categories of Health IT
Administrative Functionality

(B) *for maintaining or encouraging a healthy lifestyle*

FDA Policy for Low-Risk General Wellness Products

(C) *to serve as electronic patient records*

FDASIA Categories of Health IT
Health Management Functionality

(D) *for transferring, storing, converting formats, or displaying clinical laboratory test or other device data and results and certain other related information*

Medical Device Data System (MDDS)

(E) *to provide recommendations to health care professionals for clinical decisions, where the user can independently review the basis of the recommendation*

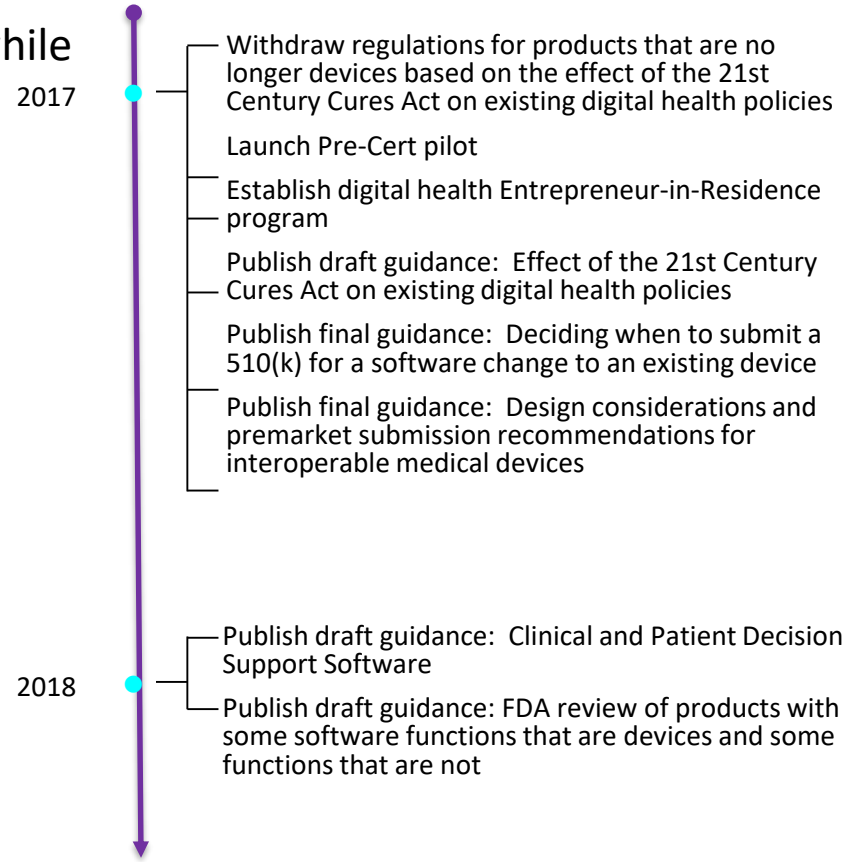
Policy for Clinical Decision Support Software included in
Health Management Functionality

Digital Health Innovation Action Plan

Re-imagining FDA's approach for bringing timely access to safe & effective digital health innovations to users

The plan lays out CDRH's vision for fostering digital health innovation while continuing to protect and promote the public health, including:

- Issue guidance conforming to software provisions of the 21st Century Cures legislation;
- Launch an innovative pilot Precertification (Pre-Cert) program to build a new approach to regulating digital health technology, working with our customers and leveraging internationally harmonized principles for software regulation; and
- Build FDA's bench strength and expertise in CDRH's digital health unit



Digital Health Innovation Action Plan

Refine policies & provide guidance

Issue guidance conforming to software provisions of the 21st Century Cures legislation

Revise regulations for products that are not devices post 21st Century Cures

2017

Publish draft guidance: Effect of the 21st Century Cures Act on existing digital health policies.

Publish final guidance: Design considerations and premarket submission recommendations for interoperable medical devices.

Publish final guidance: Deciding when to submit a 510(k) for a software change to an existing device.

Finalize the International Medical Device Regulators Forum approach to clinically evaluating SaMD.

2017

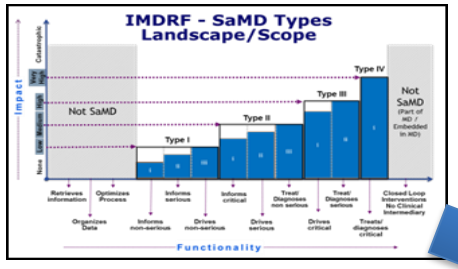
Publish draft Clinical Decision Support Software guidance that delineates the clinical decision support software that is no longer under FDA's jurisdiction

2018

Publish draft guidance: FDA review of products with some software functions that are devices and some functions that are not.

Withdraw and amend regulations for products that are no longer devices based on the effect of the 21st Century Cures Act on existing digital health policies.

Concept: *A Reimagined Approach Using FDA Pre-Cert*



Based on
SaMD Risk +
Pre-Cert level

FDA Pre-Cert level

DH
FDA Pre-Cert

e.g. lower-risk software, certain modifications

Streamlined Premarket Review

Commercial Distribution & Real-World Use

Real World Data Collection (NEST)

Regulatory Science

Real-World Evidence

Clinical Trials

Patient Preference

Outcomes research

DH
FEEDBACK

FDA Pre-Cert effectiveness feedback

Assessment effectiveness feedback

Medical Device Safety Action Plan

Outlines a vision for how CDRH can continue to enhance our programs and processes to assure:

- Safety of medical devices throughout the TPLC
- Timely identification and resolution of safety issues
- Advance innovative technologies that are safer, more effective and address unmet needs

FDA Framework for Device Oversight

The FD&C Act provides a flexible framework that takes into account that all medical devices inherently carry some risk, recognizes that “safe and effective” does not mean “risk free,” and requires that FDA tailor its oversight of devices to the degree of risk presented to provide a “reasonable assurance” of safety and effectiveness rather than an “absolute assurance”

Medical Device Innovation

Innovation and Safety

are not polar opposites but rather two sides of the same coin

Key Enhancements

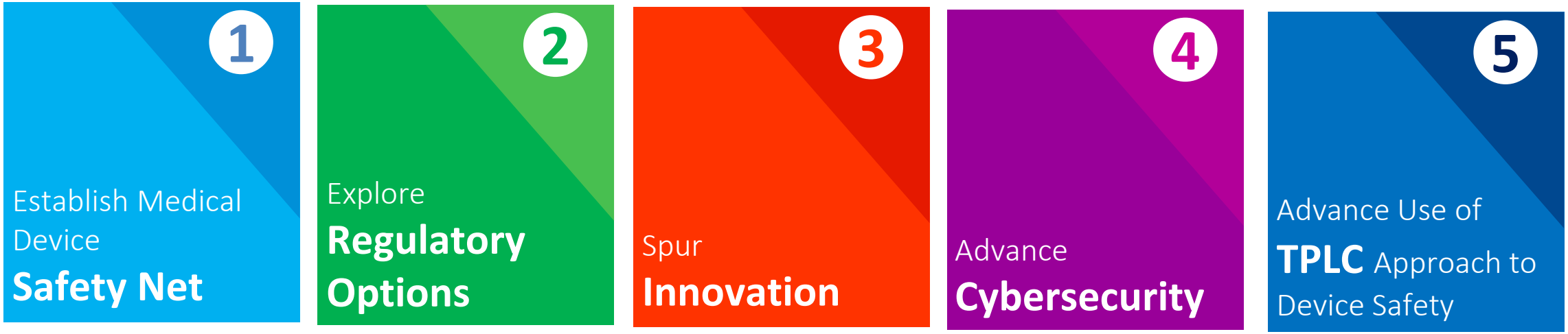
- Recalibrating the **benefit-risk framework** for device oversight in the pre- and postmarket settings
- Improving regulatory clarity regarding use of **real world evidence**
- Establishing the **unique device identification system**
- Developing the **National Evaluation System for health Technology (NEST)**
- Establishing CDRH's **Signal Management Program**
- Creating a competitive marketplace for **device quality (Case for Quality)**
- Addressing the **cybersecurity** of medical devices as a patient safety concern

Medical Device Innovation and Safety

As device technology continues to evolve we are mindful that the ways in which we assure reasonable device safety must also keep pace

And we must do so across the Total Product Life Cycle (TPLC) of a device

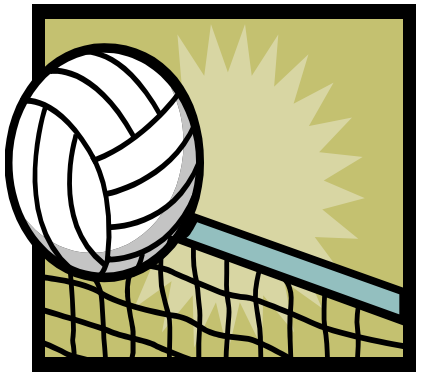
Medical Device Safety Action Plan



Medical Device Safety Action Plan

Innovation and Safety are Two Sides of the Same Coin

- Examples of Actions:
  - Work collaboratively as a member of the NEST Coordinating Center to create capabilities for active surveillance
  - Build the Women's Health Technologies Strategically Coordinated Registry Network (CRN)
  - Explore developing an umbrella regulation for safety special controls
  - Consider new cybersecurity authorities (e.g., require a Software Bill of Materials)
  - Explore a Breakthrough Device-like pathway for safer devices
  - Establish a voluntary third-party appraisal program for device quality
  - Implement Expanded Abbreviated 510(k) Program
  - Establish the Office of Product Evaluation and Quality
  - President's FY2019 Budget reflects proposals for funding to support NEST, FDA postmarket studies, and establishing a maturity model appraisal program to foster a competitive marketplace for device quality (Case for Quality)



Thank You