The State of CDRH and Future Directions

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Center for Devices and Radiological Health
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.
Flexible Regulatory Paradigms Applied Across the Total Product Life Cycle

CDRH Vision

Patient-Centered, TPLC Approach, Benefit-Risk Tradeoffs

- Postmarket Benefit-Risk Guidance (2016)

Evidence Generation

- Clinical Trials
  - Early Feasibility Study Paradigm Guidance (2013)

- Regulatory Science
  - MDDT Program

- Real-World Evidence
  - RWE Guidance (2017)
  - Unique Device Identification Final Rule (2013)

Premarket-Postmarket Balance

- Expedited Access Pathway Program (2015)

Science of Patient Input

- Patient Preference Information Guidance (2016)
- Medical Device Innovation Consortium (MDIC) Patient Centered Benefit-Risk Project

NEST

MDIC
Novel Device Approvals

* Novel devices include original PMAs, panel track supplement PMAs, and de novos

4-fold Increase in # of Novel Device Approvals

- Number of Novel Devices

Calendar Year


24 28 55 61 49 67 80 91 95
Clinical Trials (IDEs)*

>90% Reduction in Time to IDE Approval

Median number of days to full IDE approval

<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th>Median Number of Days</th>
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<tbody>
<tr>
<td>2011</td>
<td>442</td>
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<td>2013</td>
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<td>2014</td>
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<td>2015</td>
<td>30</td>
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<tr>
<td>2016</td>
<td>30</td>
</tr>
<tr>
<td>2017</td>
<td>30</td>
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* IDE=Investigational Device Exemption
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
High-Risk Devices (PMAs)

39% REDUCTION in Total Time to Decision

PMA Average Total Time to MDUFA Decision

* Cohort 89% complete; average times will increase
Moderate Risk Innovative Devices (De Novo)

67% REDUCTION in Total Time to Decision

De Novo Average Total Time to Decision*

<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th>Average Total Time to Decision</th>
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<tr>
<td>2009</td>
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<td>2010</td>
<td>666</td>
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<td>2015</td>
<td>278</td>
</tr>
<tr>
<td>2016</td>
<td>257</td>
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*Average Time to Grant, Decline, or Withdrawal

** Cohort 94.3% Complete. Average Time May Increase
Moderate Risk Devices - 510(k)

95% REDUCTION in Files that Miss Day 90
Decision within 90 FDA Days*

*Comparison of Receipt Cohorts 15 months After Start of FY
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
# 21<sup>st</sup> Century Cures Act Implementation

<table>
<thead>
<tr>
<th>Provision</th>
<th>Implementation activities completed</th>
<th>Date completed</th>
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<tbody>
<tr>
<td>Least Burdensome</td>
<td>Issued draft guidance (not mandated); trained staff</td>
<td>15 Dec 2017</td>
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<tr>
<td>CLIA Waiver</td>
<td>Issued draft guidance</td>
<td>29 Nov 2017</td>
</tr>
<tr>
<td>Breakthrough Devices</td>
<td>Issued draft guidance</td>
<td>25 Oct 2017</td>
</tr>
<tr>
<td>Classification Panels</td>
<td>Published FR Notice soliciting public input for panel membership; finalized &quot;Procedures for Meetings of the Medical Devices Advisory Committee&quot; guidance including Cures-related changes</td>
<td>23 Jun 2017 (FR notice) 1 Sep 2017 (guidance)</td>
</tr>
<tr>
<td>Cleaning &amp; Validation</td>
<td>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</td>
<td>9 Jun 2017</td>
</tr>
<tr>
<td>Central IRB</td>
<td>Published amendment to regulations removing the word “local” where needed to comply with new law</td>
<td>7 Jun 2017</td>
</tr>
<tr>
<td>Humanitarian Device Exemptions</td>
<td>Amended regulations changing the HDE population limit from 4,000 to 8,000</td>
<td>7 Jun 2017</td>
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<tr>
<td>Exemptions</td>
<td>Published lists of Class I and Class II devices exempt from requirement to submit a 510(k)</td>
<td>Final Class I list: 13 Apr 2017 Final Class II list: 11 Jul 2017</td>
</tr>
<tr>
<td>Software</td>
<td>Detailed on subsequent slides</td>
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</table>
Breakthrough Device Pathway (Formerly Expedited Access Pathway)

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** - Straightforward 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
NESTcc surveyed current data partners on their data capabilities to determine current capabilities, gaps, and priority areas.

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

Data partners represent:
- 56 Hospitals
- 250 Outpatient Clinics

Patient data represents:
- Patient Records: 149M+
- Unique Patient Encounters: 344M+

Partners report regular data refreshes:
- 2 Daily
- 3 Monthly
- 2 Mixed Rates
- 4 Quarterly

Most cited expertise:
- Cardiovascular and Cardiac Surgery
- Women’s Health
- Neurosurgery
- Gastroenterology
- Orthopedic
**DEVELOP NESTcc’S ROLE, CONT’D**

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.
RWE Use Proof of Concept

Premarket Examples

• New Product Approvals, Clearances, Humanitarian Device Exemptions (HDEs) and Grants of De Novo
  – Drug-eluting stent
  – Pacing leads
  – Spinal cord stimulation system
  – Pressure wedge for the reduction of cesarean delivery
  – Esophageal cooling device
  – Companion diagnostic
  – IVD for cystic fibrosis
  – Esophageal atresia anastomosis device

• Expanded Labeling Indications
  – Ventricular support device
  – Cardioverter defibrillator
  – Drug coated balloon catheter
  – Excimer laser (LASIK)
  – Bioprosthetic pulmonary valve
  – Transcatheter heart valve

• Conversion of HDE to Premarket Approval
  – Pediatric ventricular assist device
Transcatheter Heart Valves
The Road from 42nd

**U.S. 42nd Country to Approve a 1st Generation TAVR Device**

**TVT Registry**
Established at Time of Device Approval

**CMS NCD**
FDA approval of subsequent indications automatically covered

**TVT Registry**
Used to Support Approval of Subsequent Indications and Device Generations

**3rd Generation TAVR for Intermediate Risk**
18 days after CE Mark for similar device

**Mitral Valve-in-Valve**
1st in World
Transcatheter Heart Valves
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Return on Investment (ROI)
3 companies invested total of $24M
19 Decisions: Studies would have cost ~$147M
ROI > 400%
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”
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

- Foster organic connections within the organization
- Streamlined decisions and processes
- Shared priorities
- Better customer service
- Professional growth
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?
Continued Use of Flexible Regulatory Approaches

Examples include:

- Focus on Least Burdensome → Simplicity
- Premarket-Postmarket Shift
- Use of Real World Evidence → NEST
- Enhanced Use of Consensus Standards
- Appropriate Level of Uncertainty
- Expanded Abbreviated 510(k) Program
- Expanded Use of Special 510(k)s
- Next Generation Sequencing Test Paradigm
- Digital Health Pre-Certification Program
- Case for Quality Maturity Model Appraisal Program
- Medical Device Single Audit Program (MDSAP)
- International Harmonization → Medical Device Single Review Program
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
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
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
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

2017
Withdraw regulations for products that are no longer devices based on the effect of the 21st Century Cures Act on existing digital health policies
Launch Pre-Cert pilot
Establish digital health Entrepreneur-in-Residence program
Publish draft guidance: Effect of the 21st Century Cures Act on existing digital health policies
Publish final guidance: Deciding when to submit a 510(k) for a software change to an existing device
Publish final guidance: Design considerations and premarket submission recommendations for interoperable medical devices

2018
Publish draft guidance: Clinical and Patient Decision Support Software
Publish draft guidance: FDA review of products with some software functions that are devices and some functions that are not
Concept: A Reimagined Approach Using FDA Pre-Cert

Based on SaMD Risk + Pre-Cert level

FDA Pre-Cert level

Streamlined Premarket Review

e.g. lower-risk software, certain modifications

Commercial Distribution & Real-World Use

Real World Data Collection (NEST)

DH FEEDBACK

FDA Pre-Cert effectiveness feedback

DH Pre-Cert

FDA Pre-Cert

Assessment effectiveness feedback

IMDRF - SaMD Types Landscape/Scope

SaMD Risk + Pre-Cert level

Streamlined Premarket Review

FDA Pre-Cert

FEEDBACK

DH

Regulatory Science

Real-World Evidence

Clinical Trials Outcomes research

Patient Preference
Medical Device Safety Action Plan

1. Establish Medical Device Safety Net
2. Explore Regulatory Options
3. Spur Innovation
4. Advance Cybersecurity
5. Advance Use of TPLC Approach to Device Safety
Medical Device Safety Action Plan
Innovation and Safety are Two Sides of the Same Coin

• Apply a TPLC approach for patient safety
• Spur innovation to address unmet patient needs and develop safer, more effective devices

• Examples of Actions:
  – Work collaboratively as a member of the NEST Coordinating Center to create capabilities for active surveillance
  – 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
  – 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)
Achieving Our Vision

**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.

P. Focused
Collaborative Communities
Innovative Approaches
Thank You