FDA as Innovator: Reimagining the Medical Device Oversight Paradigm

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Center for Devices and Radiological Health
U.S. Food and Drug Administration
November 1, 2018
Patients are at the Heart of What We Do

Updated CDRH Mission, Vision and Shared Values

2012

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.
FDA as Innovator: Strategy

• Revolutionize the Evidence Generation Paradigm

• Transform the Device Regulatory Framework

• Evolve the Role of the FDA
Better Tailored, More Consistent Benefit-Risk Determinations Supporting Our Decision-Making

- 2012: Premarket Guidance (Draft) 510(k)s
- 2013: Premarket Guidance (Final) Premarket Approval (PMA) and De Novo Classifications
- 2014: Premarket Guidance (Final) Investigational Device Exemptions
- 2015: Postmarket Guidance (Final) Medical Device Product Availability, Compliance and Enforcement Decisions
- 2016: Postmarket Guidance (Final)
- 2017: Premarket Guidance (Final)
Customer Service Oriented

- Customer Service Standards of Excellence
- Customer Service Training
- Customer Service Surveys
- FEEDBACK ✓ CDRH
- CDRH Quality Management Framework

90% Customer Satisfaction
M3 Foundational 510(k) Policies

- Refuse to Accept Policy
- Substantive Review
- Interactive Review
- “No Submission Left Behind”
- Issuance of 510(k) Program Guidance
## Premarket Performance Highlights

<table>
<thead>
<tr>
<th>90% Reduction</th>
<th>Time to Full IDE Approval</th>
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<tbody>
<tr>
<td>Since 2011</td>
<td>Mean = 30 days</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>36% Reduction</th>
<th>PMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Since 2009</td>
<td>Total Time to Decision</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>67% Reduction</th>
<th>De Novo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Since 2009</td>
<td>Total Time to Decision</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>95% Reduction</th>
<th>510(k)s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Since 2010</td>
<td>That Miss Day 90</td>
</tr>
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</table>
Novel Device Approvals

~4-fold Increase in # of Novel Device Approvals

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

Calendar Year


24 28 55 61 49 67 80 91 95

Graph showing the increase in novel device approvals from 2009 to 2017.
Application of Least Burdensome

- 21st Century Cures updated the LB provisions and requires training of FDA staff
- CDRH believes LB applies to all activities related to medical device regulation
- Draft Guidance issued December 15, 2017

The minimum amount of information necessary to adequately address a regulatory question or issue through the most efficient manner at the right time.
Developing and Responding to Deficiencies in Accordance with Least Burdensome Provisions

Guidance Issued - September 29, 2017

• Major deficiencies:
  - If not resolved, will preclude a favorable decision on the application; their resolution is necessary in order to reach a final

• Minor deficiencies:
  - Requests that can be resolved in a straightforward manner, but that need to be addressed to meet regulatory requirements or to prevent potential misbranding or adulteration
    - Resolved interactively whenever possible

• Additional Considerations:
  – Suggestions, recommendations, or requests that are not expected to preclude a favorable decision on the marketing application
    – Do not require an applicant response
Strategies to Reduce 510(k) Total Time to MDUFA Decision

New Policies

- RTA Addendum: Notifies Applicant of issues earlier in review
- Day-10 Call: Provides clarification prior to final review cycle
- Branch-level SE: Reduces time waiting for Division level sign off and review
- First Round NSE: Addresses NSE issues earlier in review cycle

Goal: Decrease TTD
Least Burdensome Flag

- Opportunity for sponsor to “throw flag” during review
- Must have made good faith effort to resolve with review team and management
- Triggers senior management review of focused clinical/scientific issue
- 3 week timeline for resolution of issue
SMART Template

- Formatted guide/template for review staff
- Promotes consistency in review and documentation
- Includes links to help/advice to facilitate review
## Device/System Description

### Device Characteristics

<table>
<thead>
<tr>
<th>Device Characteristics</th>
<th>Inadequate Or Marked</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the intended use or fundamental technology new?</td>
<td>No</td>
</tr>
<tr>
<td>Is the device life-supporting or life sustaining?</td>
<td>No</td>
</tr>
<tr>
<td>Are there any direct or indirect patient contacting components?</td>
<td>Yes</td>
</tr>
<tr>
<td>• Is the device or a component an implant?</td>
<td>Yes</td>
</tr>
<tr>
<td>Does the device use software/firmware?</td>
<td>No</td>
</tr>
<tr>
<td>Does the device or a component need sterilization (by manufacturer or user)?</td>
<td>Yes</td>
</tr>
<tr>
<td>The device/system uses or is...</td>
<td>a single use device(s) (SUD)</td>
</tr>
<tr>
<td>The environment of use of the device/system includes...</td>
<td>Professional Healthcare Facility</td>
</tr>
<tr>
<td>Is the device a combination product?</td>
<td>N - Not a Part 3 Combination Product</td>
</tr>
<tr>
<td>Is the device/system electrical (battery or wall powered)?</td>
<td>No, the device is not electrical</td>
</tr>
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Check the attributes that are applicable to this submission.

<table>
<thead>
<tr>
<th></th>
<th>Nanotechnology</th>
<th>Reprocessed SUD</th>
<th>Companion Diagnostic</th>
<th>Medical Counter Measures</th>
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<td>Unknown</td>
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Device Description Table: Summary of important device characteristics
Quality in 510(k) Review Pilot Program

• “Turbotax” for 510(k)
• Sponsor completes formatted eSubmission
• In return, CDRH will:
  • Skip RTA phase
  • Commit to interactive review without hold
  • Reduce FDA review time by 1/3

Launched Pilot for Selected Product Codes
September 6, 2018
Breakthrough Device Pathway  
(Formerly Expedited Access Pathway)

96 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

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.
Improving 3rd Party Review Program

• Program Challenges:
  • Poor quality submissions that often require re-review
  • Limited public information makes review difficult

• Plans to Strengthen Program:
  • Issued draft guidance on recognition of third parties and a strategy for not routinely re-reviewing 510(k)s reviewed by a third party on September 13, 2018
  • Increase program staff from 1 to 5 FTEs
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

Draft Guidance Proposing Expanded Use 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
- Provides opportunities for international harmonization, where appropriate, and supports the establishment of a Medical Device Single Review Program
Consideration of Uncertainty In Making Benefit-Risk Determinations in PMA, De Novo, and HDE Approvals

- 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

Clarified Through Draft Guidance Issued on September 5, 2018

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

Provides opportunities for international harmonization, where appropriate, and supports the establishment of a Medical Device Single Review Program
Foundational Work on NEST
Key Features of NEST

Purpose: To drive down the time and cost and increase the value and use of real-world data to meet the needs of medical device ecosystem stakeholders through a market-driven, collective buying power approach and using a neural network data model:

- **Independent Coordinating Center** responsible for driving standardization of core data elements, data quality, use of common definitions, linkages between data sources, development of advanced analytics, and creating data use agreements as conditions of data sources participating in NEST

- **Overseen by a Governing Committee** comprised of representatives of ecosystem stakeholders that is responsible for establishing NEST’s policies and procedures, setting strategic direction and priorities, and directing investments by the Coordinating Center

- **Business Model:**
  - Base funding from private and public sector sources
  - NEST users pay for access to and analysis of data from participating NEST data sources
  - Success requires demonstrating ROI, e.g., less expensive, more timely to use NEST

- “**Minimum Viable Product**” by December 31, 2019
NESTcc surveyed its Data Network to determine current capabilities, gaps, and priority areas.

Survey respondents represent:

- 195 Hospitals
- 3,942+ Outpatient Clinics

Patient data represents: 495M+

Common data models:
- I2b2
- OMOP
- PCORnet
- Sentinel

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

Most cited expertise:
- Cardiovascular and Cardiac Surgery
- Women’s Health
- Neurosurgery
- Gastroenterology
- Orthopedic
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

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

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

**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

The Road from 42\textsuperscript{nd}

- U.S. 42\textsuperscript{nd} Country to Approve a 1\textsuperscript{st} 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
- 3\textsuperscript{rd} Generation TAVR for Intermediate Risk
  18 days after CE Mark for similar device
- Mitral Valve-in-Valve 1\textsuperscript{st} in World

Return on Investment (ROI)

- 3 companies invested total of $25M
- 22 Decisions: Studies would have cost \textsim\$134M
- 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

- Payer Presubmission Participation
- Opportunity to Obtain Payer Input

Current Participants:
- BlueCross BlueShield Association
- Centers for Medicare and Medicaid Services
- Duke Evidence Synthesis Group
- ECRI Institute
- Humana
- Kaiser Permanente
- National Institute for Health and Care Excellence
- United Health Group
- CareFirst

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

For more information: Google Search “CDRH Payer Program”
Medical Device Single Review Program

- Leverage work products for and learnings from the Medical Device Single Audit Program

- IMDRF Good Regulatory Review Practices WG
  - Competence, Training, and Conduct Requirements for Regulatory Reviewers Final Document
  - Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices Final Document
  - Principles of Labeling Proposed Document
  - New Work Item: Recognition of Entities Performing Premarket Review

- Programmatic Changes in CDRH

- NEST
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
Establish a robust medical device patient safety net in the United States

- Work collaboratively as a member of the NEST Coordinating Center’s Governing Committee to create capabilities for active surveillance
- President’s FY2019 Budget reflects a proposal for funding to support NEST and CDRH postmarket studies
- Build the Women’s Health Technologies Strategically Coordinated Registry Network (CRN)
- Leverage existing CRNs to evaluate sex/gender differences and long-term safety for devices in multiple clinical areas
CDRH Reorganization: Office of Product Evaluation and Quality
Total Product Lifecycle (TPLC) Reorganization

- Foster organic connections within the organization
- Streamlined decisions and processes
- Shared priorities
- Better customer service
- Professional growth
## Future OPEQ Offices

<table>
<thead>
<tr>
<th>OHT</th>
<th>Scope of Products / Responsibilities</th>
<th>Office Director</th>
</tr>
</thead>
<tbody>
<tr>
<td>OHT 1</td>
<td>Ophthalmic, Anesthesia, Respiratory, ENT and Dental Devices</td>
<td>Malvina Eydelman, M.D.</td>
</tr>
<tr>
<td>OHT 2</td>
<td>Cardiovascular Devices</td>
<td>Bram Zuckerman, M.D.</td>
</tr>
<tr>
<td>OHT 3</td>
<td>Reproductive, Gastro-Renal, Urological, General Hospital Device and Human Factors</td>
<td>Ben Fisher, Ph.D.</td>
</tr>
<tr>
<td>OHT 4</td>
<td>Surgical and Infection Control Devices</td>
<td>Binita Ashar, M.D.</td>
</tr>
<tr>
<td>OHT 5</td>
<td>Neurological and Physical Medicine Devices</td>
<td>Carlos Pena, Ph.D.</td>
</tr>
<tr>
<td>OHT 6</td>
<td>Orthopedic Devices</td>
<td>Raquel Peat, Ph.D., MPH</td>
</tr>
<tr>
<td>OHT 7 /OIR</td>
<td>In Vitro Diagnostics and Radiological Health</td>
<td>Tim Stenzel, MD, PhD</td>
</tr>
<tr>
<td>ORP</td>
<td>Programmatic oversight for premarket, postmarket and compliance activities</td>
<td>CAPT Sean Boyd</td>
</tr>
<tr>
<td>OCEA</td>
<td>Programmatic oversight for clinical trial, BIMO, RWE, and statistical activities</td>
<td>Owen Faris, PhD</td>
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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

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
Putting the Pieces Together: The Whole is Greater than the Sum of its Parts
### 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
Balancing Innovation and Patient Safety with Foundational Policies

www.fda.gov
Leading International Convergence effort on Software as a Medical Device (SaMD)

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

Based on SaMD Risk + Pre-Cert level

Commercial Distribution & Real-World Use

Streamlined Premarket Review

e.g. lower-risk software, certain modifications

FDA Pre-Cert level

DH FDA Pre-Cert

Assessment feedback

DH FEEDBACK

FDA Pre-Cert effectiveness feedback

Real World Data Collection (NEST)

Regulatory Science

Real-World Evidence

Clinical Trials Outcomes research

Patient Preference
Learning Medical Device Ecosystem

Total Product Life Cycle (TPLC) Framework

Total Product Life Cycle Framework

- **Benefit-Risk Evidence**
  - Progressive Approval, Safety and Performance
  - Benefit-Risk
  - Patient Access

- **International Harmonization**
  - NEST
  - Clinical Research Incorporated Into Routine Clinical Practice

**TIME TO MARKET**

- **Premarket Review**
  - Premarket Decision
  - Benefit-Risk

**INFORMATION FLOW**

- "Safety Net"
Thank You