CDRH Update

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Food and Drug Administration

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

The U.S. is the world’s leader in regulatory science, medical device innovation and manufacturing, and radiation-emitting product safety.

U.S. post-market surveillance quickly identifies poorly performing devices, accurately characterizes real-world performance, and facilitates device approval or clearance.

Devices are legally marketed in the U.S. and remain safe, effective, and of high-quality.

Consumers, patients, their caregivers, and providers have access to understandable science-based information about medical devices and use this information to make health care decisions.
Pubic Health and Patients are a Priority

• CDRH’s congressionally mandated Mission has two pillars: To **Protect** and **Promote** public health

• Our safety efforts help us protect public health by assuring that medical devices are high-quality, safe and effective and that we identify and address safety issues **first in the world**

• Our innovation efforts help us promote public health by advancing device (value-added) innovation and assuring patients have timely access to high-quality, safe and effective medical devices of public health importance **first in the world**
The Misperception

SAFETY AND INNOVATION

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

Ensure that FDA is consistently first among the world’s regulatory agencies to identify and act upon safety signals related to medical devices

Published on FDA website April 12, 2018
Strengthening the Innovation Pipeline

>90% Reduction in Time to Clinical Trial (IDE) Approval

Median # days to full IDE approval

>4-fold Increase in # of Novel Device* Approvals

* Novel devices include original PMAs, panel track supplement PMAs, de novos, HDEs and breakthrough 510(k)s
MDIC AND CDRH COLLABORATIVE EFFORTS

OVER 100 FDA STAFF CONTRIBUTORS
MDIC: Science of Patient Input (SPI)

Goal: to improve our ability to include patient perspectives in the development, pre-market approval, and post-market evaluation of medical devices

Heart Failure Patient Preference Study

- Developing a survey to understand patient preferences for novel heart failure devices
- Potential to provide an example of how to do a PPI study in the pre-competitive space with multiple industry sponsors, patients and regulators
- Understanding patient preferences can help advance innovation and benefit/risk assessments for new heart failure devices

Framework of Patient Input in Medical Device Clinical Trials

- Developing resources for industry to use to foster patient engagement in clinical investigations
  - Best Practices for Communicating Benefit, Risk, and Uncertainty white paper (available for comments through Sept. 13)
  - Literature Review of Patient Engagement in Clinical Trials
  - Patient Engagement in Clinical Trials Survey Report
The Patient Science and Engagement program’s objective is to understand the patients’ perspectives and proactively incorporate it in our regulatory efforts

• **17** industry sponsored PPI studies completed or in the pipeline
  – To identify clinical trial outcomes and performance goals
  – To inform benefit/risk assessments, some leading to label expansion

• Issue draft guidance on Patient Engagement in Clinical Investigations

• Increasing number of PROs being listed as primary or secondary endpoints in medical device clinical investigations

• Developing models for adapting or modifying (“bridge”) PRO measures and drafting guidance on flexibility in generating validity evidence for PRO measures
MDIC: Clinical Diagnostics (CDx)

**Goal:** Foster innovation and speed patient access to new IVD tests by developing new tools and methods that will improve processes to assess safety, effectiveness and the value proposition of diagnostic tests.

**Framework for Developing Clinical Evidence for Regulatory and Coverage Assessments in In Vitro Diagnostics (IVDs) Published August 2019**

- Includes a library of frequently used tests to demonstrate analytical validity, assay types and measurements of clinical validation
- Explores strategies for developing clinical utility evidence for payers
- Offers planning resources
- May help test sponsors decide how to develop credible evidence of analytical and clinical validity and utility
CDRH: Clinical Diagnostics (CDx)

Surrogate Samples and Clinical Evidence Framework Benefits

**Manufacturers**
- Effective use of resources
- Avoid repeating analytical studies because of use of inappropriate surrogate samples
- Less time for analytical validation
- Better information about assay performance for the *patient* samples
- An initial thought piece about the entire process starting from development till coverage
- Especially useful for small companies
- Some steps can be performed in parallel

**FDA Reviewers**
- More consistency
- Faster review
- Especially useful for new reviewers

**Physicians**
- Information in labeling reflects performance of the assay with the patient samples

**Patients:**
- Faster access to better diagnostic tests
MDIC: Early Feasibility Studies (EFS)

EFS Site Network Pilot Update:

Goal: To develop a national EFS learning system

- Launching point: Network of high-performing EFS sites
  - Nation-wide coverage
  - Expansion to multiple therapeutic areas
- Currently over 30 leading clinical sites
  - Survey underway
- “Learning Environment”
  - Breaking down barriers to learning between sites, sponsors & stakeholders
- Informed Consent Template: Workshop in October
### Early Feasibility Studies:
#### Perceptual Shifts in Ease of Conduct

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*Data provided by Aaron Kaplan/Dartmouth Device Development (3D) Symposium Annual Survey of 3D Participants*
CDRH: Early Feasibility Studies (EFS)

- More than a doubling of IDEs submitted over past 6 years
- Over 200 EFS have been approved to treat/diagnose >2500 patients
- Staff facilitation transition to pivotal trials
  - Early discussions with Sponsors
  - Transparency non-clinical testing to support pivotal study IDE
- CDRH is focused on sustainable EFS program growth across all therapeutic areas
**MDIC: External Evidence Methods (EEM)**

**Goal:** to establish a more predictable pathway for use of external evidence methods (EEM)

- Collaborate with the Computational Modeling and Simulation (CM&S) MDIC Workstream
  - Quick and predictable access for patients to innovative technologies, enabled by computation modeling and simulation evidence of safety and performance
  - Virtual Patients as a New Source of Evidence

**External trial data:**
- Real-world data (RWD)
- Real-world evidence (RWE)
- Computational Modeling and Simulation (CM&S)
- Similar device clinical trial data

**What’s Next:**
- Cataloging of existing methods for evidence fusion from data external to a clinical trial
- Development of CM&S tools to use as external evidence

To support regulatory medical device decisions and other stakeholder decisions
CDRH: *In Silico* Trials for Regulatory Evaluation

Holds promise for evaluating the safety and efficacy of imaging technologies with less burden compared to clinical investigations

- Diagnostic study used computer-simulated imaging of 2,986 synthetic image-based virtual patients to compare two types of breast cancer screening technologies. Does the in silico trial mirror the real study?
- Outcome: Same regulatory decision with the *in silico* trial lasting 1.75 years instead of 4 year comparative trial using many more people exposed to ionizing radiation

Each image is a simulated mass-containing region from a simulated breast cancer subject.

Traditional pathway for gathering high quality clinical data:

- Requires prospective enrollment in trials and other studies
- Utility is often limited by high cost
- Long completion timeline
- Poor applicability to the real-world diversity of patient characteristics and medical practitioner skills and experience.

NEST will reduce the time and cost of evidence generation via the traditional pathway while assuring the development and use of sound science and the implementation of adequate patient protections for patient-centered regulatory decision making

- Draft framework documents released for public comment (May 2019)
- Writing group finalization of frameworks (September 2019)

FDA subject matter experts serving as PIs on 2 NESTcc Demonstration Projects
Multi-Stakeholder Engagement

• Analyze registry data linked to administrative claims to assess the real world and long-term device performance

• Assess late mortality signal after treatment with paclitaxel-coated balloons and paclitaxel-eluting stents used to treat peripheral artery disease using data sources including:
  – Private payor and Medicare administrative claims
  – National Registries
  – Meta-analyzed clinical trials data

• Members on the NESTcc Active Surveillance Task Force creating a Roadmap for incorporating active surveillance activities in their partner network

NEST will foster our ability to be first in the world for novel device approvals and signal detection
Goal: Advance the quality and safety of the medical devices market in the United States

Voluntary Improvement Program (CfQ VIP)

• Launched a quality maturity appraisal pilot in January 2018
  – Engaged various stakeholders in the ecosystem and outside the medical device industry.
  – Learned and pivoted multiple times in 2018
  – Initiated new projects to address opportunities for improvement

• Pilot successes and impact
  – Shifted inspection resources on 45 sites
  – Reduced 30-Day notice review to less than 5 business days. Average is 2.8 days.
  – Measurable patient impact and business value demonstrated.

• Pilot is continuing in 2019, developing components for an operational program

- 24 participating firms (51 sites enrolled, 46 active)
- >50 appraisals (12 reappraisals after 1 year)
- 86% report appraisal had a positive impact on product quality
- 12% average appraisals improvement after 1 year
Goal: Advance cybersecurity across the medical device ecosystem in support of patient safety by leveraging multi-stakeholder engagement and developing novel regulatory science tools and methods

Cybersecurity is integral to US critical infrastructure; MDIC can provide unique collaboration solutions to
• Define medical device cybersecurity research priorities
• Identify approaches for communicating cybersecurity considerations to patients
• Develop a language library for cybersecurity through a TPLC lens
• Build resources and develop tools to address current cybersecurity skills gap in medical device industry workforce

Coordinated Vulnerability Disclosure (CVD) Project
• Report on Advancing Coordinated Vulnerability Disclosure (Oct 2018)
• Hypothetical, Interactive Case Study on CVD - Educational Video/ MDICx (Nov 2018)

Threat Modeling for Medical Device Sector
(Project Scoping Phase)
• Bootcamp series
• Playbook
• Educational Resources

Collaborative effort between FDA, MDIC industry members, ISAOs, SMEs from other sectors
CDRH: Medical Device Cybersecurity

Updates to the Content of Premarket Submissions for Management of Cybersecurity in Medical Devices Guidance Document

- Lessons learned from routine vulnerability management, response activities, engaging stakeholders
- Working with manufacturers pre- and post-market

Define and operationalize Software Bill of Materials

- Multi-stakeholder engagement

Complete new IMDRF work item

- Draft guidance on TPLC approach to medical device cybersecurity

#WeHackers

- A collaborative movement between the medical device and security researcher communities
- Ten device manufacturers declaring their intent to bring their devices to DEF CON’s Biohacking village
CDRH Staff Involved in MDIC Work

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Ash Rao
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Toby Lowe
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Weijie Chen
Xu (Sherry) Yan
Xuefeng Li
You Li
Yun-Fu Hu
Yun-Ling Xu
Zivana Tezak
For the device industry to successfully innovate and for the FDA to optimally safeguard the public, the FDA must be supported - to be innovative.
Is the 40+ year old regulatory framework for medical devices still fit for purpose today?
Digital Health Program

Unified and collaborative environment; applying best practices, conducting research, support, training for software and digital health technologies.

Supplementing bench strength @ FDA

TECH POLICY SUPPORT

- Manage/Respond to Inquiries
  - Regulatory Submissions Support
  - Policy Implementation
  - Identify and develop staff training

CENTER OF EXCELLENCE

POLICY DEVELOPMENT

Explore tailored pathway: Software Precertification Pilot
- Medical Device Interoperability
- Cybersecurity

Strategic Partnership: harmonization through IMDRF
- Strategic Industry partnership
- Academic partnership
- Federal partnerships:

STRATEGIC INITIATIVES

Cybersecurity Interoperability
- Artificial Intelligence / Machine Learning
- Software Policies under 21st Century Cures Act
- Policy Intelligence

STRATEGIC PARTNERSHIP

Cybersecurity
- Interoperability