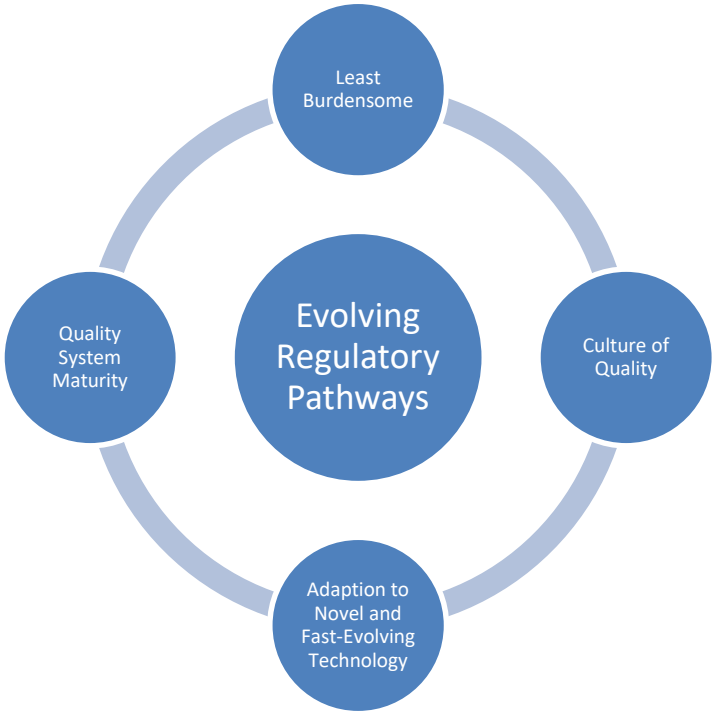
Evolving Regulatory Pathways for Medical Devices

CDRH Policy Perspective/Key Initiatives

- CDRH 2018-2020 Strategic Priorities
  - Simplicity & Collaborative Communities
- Implementing statutory changes, Cures & FDARA
- Regulatory Reform efforts
- Innovative Approaches, such as being explored through Digital Health activities
- Safety Action Plan

Key Themes


Focus
on
Quality


Least Burdensome
Culture of Quality
Adaption to Novel and Fast-Evolving Technology
Quality System Maturity
Evolving Regulatory Pathways

Common Thread: Least Burdensome

"Least Burdensome" Initiatives

"FDA believes … that least burdensome principles should be consistently and widely applied to all activities in the **premarket and postmarket settings** to remove or reduce **unnecessary burdens** so that patients can have earlier and continued access to **high quality, safe, and effective devices**"

- Pre-Cert Pilot
- Digital Health Guidances:
  - Mobile Medical Applications Guidance
  - General Wellness: Policy for Low Risk Devices Guidance
  - Clinical and Patient Decision Support Software Draft Guidance
  - Changes to Existing Software Policies Resulting from Section 3060 of 21st Century Cures Act Draft Guidance
  - Multiple Function Device Products Draft Guidance
- Intent to Exempt Certain Devices Guidance & Exemptions from 510(k): Class II Devices Final Rule
- Use of RWE to Support Regulatory Decision-Making for Medical Devices Guidance
- Benefit-Risk Guidances
- Expansion of Abbreviated 510(k) Program: Demonstrating SE through Performance Criteria Draft Guidance
- FDA requirement to publish a LB audit per Cures (Congressional report)

FDA Guidances

- **The Least Burdensome Provisions: Concept and Principles**
  - Draft; issued on 12/15/2017; comments closed; to supersede prior guidance issued on 10/4/2002
- **Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions**
  - Final; issued on 9/29/2017; supersedes prior guidance issued on 11/2/2000
- **Statutory bases**: Food and Drug Administration Modernization Act (FDAMA) (1997); Food and Drug Administration Safety and Innovation Act (FDASIA) (2012); 21st Century Cures Act (2016)

New Definition of "Least Burdensome"

- **Old** – "a successful means of addressing a premarket issue that involves the most appropriate investment of time, effort and resources on the part of industry and FDA"
- **New** – "the minimum amount of information necessary to adequately address a regulatory question or issue through the most efficient manner at the right time (e.g., need to know versus nice to know)"

"Least Burdensome" Guidance – Guiding Principles

- Minimum information necessary
  - Less burdensome sources of clinical data (e.g., RWE, literature, OUS data)
  - Non-clinical data
  - Alternative approaches
- Most efficient means to resolve issues
  - Reduce burden of traditional clinical studies (e.g., historical control groups, registry data)
  - Use benefit-risk assessments
  - Streamline processes and reduce administrative burden
  - Smart Regulation
  - Global harmonization
- The right time
  - Balance pre- and post-market information needs

Streamlining Process for Device Iterations and Adapting to Novel and Fast Evolving Technology

Deciding When to Submit a 510(k) for a Change to an Existing Device

- Required when a change could significantly affect safety or effectiveness; major changes in intended use
- Not intended to implement significant policy changes
- Intended to enhance predictability, consistency and transparency in the process and establish more clarity for when FDA need to review changes

Deciding When to Submit a 510(k) for a Change to an Existing Device

- Adds clarity regarding when changes to indications require a new 510(k)
- Added a risk-based assessment approach
- Added documentation recommendations and examples
- FDA also released a separate guidance regarding deciding when to submit a 510(k) for software changes, based on same key principles

Draft Guidance - Expansion of Abbreviated 510(k) Program: Demonstrating Substantial Equivalence through Performance Criteria

- **Proposed Optional Pathway; Intended for well-understood device types**
- Would allow applicants to demonstrate safety and effectiveness by meeting FDA-identified performance criteria
  - Identification of predicate, but direct head-to-head comparisons against predicate devices would not be required to demonstrate substantial equivalence

Draft Guidance - Expansion of Abbreviated 510(k) Program: Demonstrating Substantial Equivalence through Performance Criteria

- FDA to maintain list of device types appropriate for program on FDA website
- Guidances to identify performance criteria for each device type, as well as testing methods where feasible
  - Consensus standards; special controls
  - Criteria to represent performance levels that are at least equivalent to performance of marketed devices of device type

Digital Health

- Digital Health Innovation Action Plan (July 2017)
  - Launched FDA's DH software pre-cert pilot program
  - New guidances to modernize FDA policies & promote innovation
  - Increasing DH staff
- Progress Update on Pre-cert program (April 2018)
  - Working model of the program
  - List of Challenge Questions
  - Please submit your feedback

Additional Areas of Evolution in Device Regulation

- Breakthrough Devices
  - Getting innovative devices to market
  - Voluntary program for certain devices that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions
- Real World Evidence

Streamlining Premarket Process with Focus on Quality

PMA CtQ Pilot Program - Overview

- **Voluntary Premarket Approval Application (PMA) program**
  - Open to first 9 eligible applicants through 12/31/2018
- **GOAL:** To **promote quality** in device design and manufacturing and to **streamline** the PMA process
  - Assuring that quality system includes rigorous controls for characteristics critical to safety and effectiveness
- **PROCESS:**
  - Proactively engage with FDA to identify CtQ device and manufacturing characteristics critical to product quality, which may include specific device features or quality control practices
- **REGULATORY PROCESS MODIFICATIONS:**
  - More focused post-approval inspection instead of standard preapproval inspection
    - Focus on implementation of design, manufacturing, and quality assurance practices identified in PMA

Manufacturing and Product Quality Pilot Program

- **Voluntary '*Case for Quality Maturity Model*' pilot program**
  - Currently enrolling interested participants
- **GOAL:** To **improve product quality** in the field by enabling **continuous improvement and organizational excellence** above & beyond compliance among manufacturing sites
- **PROCESS:**
  - 3rd party teams certified by Capability Maturity Model Integration (CMMI) Institute will conduct maturity model appraisals
  - Manufacturing sites will demonstrate continued pursuit of improvement to CMMI
  - Manufacturing sites will identify key quality metrics to share with FDA
- **REGULATORY PROCESS MODIFICATIONS:**
  - Forego conducting surveillance and preapproval inspections for participating sites
  - Streamlined 30 Day Notice, PMA, and Product Transfer submission forms & expedited approvals.

Current pilot key statistics

Applications

20 Qualified

2 Withdrawn

16 US

4 OUS

Appraisals

11 Completed

2 Scheduled

3 In scoping

2 New Enrollees

1 Multi-site In scoping

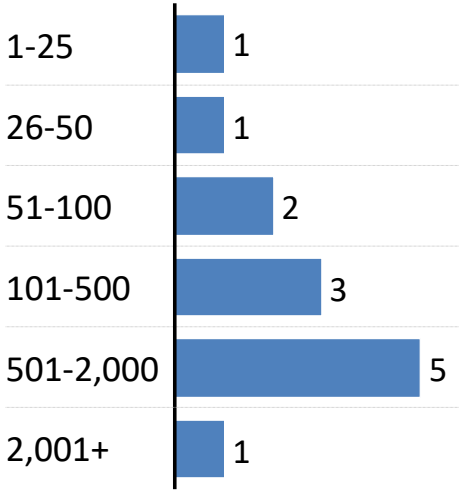
Diverse product classification mix

Class I	1
Class II	3
Class III	3
Class I and Class II	3
Class II and Class III	8
All classes	2

Inspection modifications started

- 2 instances where inspection occurred despite application
- No additional issues since new internal communication process established

Diverse pilot participant site size (by employees)



Modified change submissions started

- 2 received – accepted in 48 hours
- Need to revise to 2 business days
- One new PMA review with waived preapproval inspection

Combination Products

Combination Product Process

- FDA working to improve combination product review process – most notably inter-center consults
- Established Combination Products Policy Council – SMG 2010.17
- Expectations and Procedures for Engagement Among Medical Product Centers and OCP on Combination Products Regulations and Guidance – SMG 4103
- Changes under 21st CC and PDUFA VI for combination products, especially in process
- Pain points still exist: human factors, inconsistency of review

Hatch-Waxman for Combination Products Using an Already-Approved Constituent Part

- 21st Century Cures created new requirements for CDRH-led combination products that have drug constituent part that is already approved
- Sponsor must:
  - Submit patent certification – PI - PIV.
  - 30-month stay applies if suit is timely brought.
- Exclusivities for the drug also block approval of the combination product.
- 510(k) & PMA RTA guidances reflect these requirements.