

# FDANews Medical Device Quality Congress

*FDA Medical Device Regulation Agenda:*

*Are you Prepared?*

April 23, 2019

**PRESENTED BY:**

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# Agenda

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- CDRH Reorganization
- CDRH Guidance Agenda, FY 2019
- FDARA Update
- Overview of Recent Postmarket Policies and Pilots
- Looking Ahead



# CDRH Reorganization

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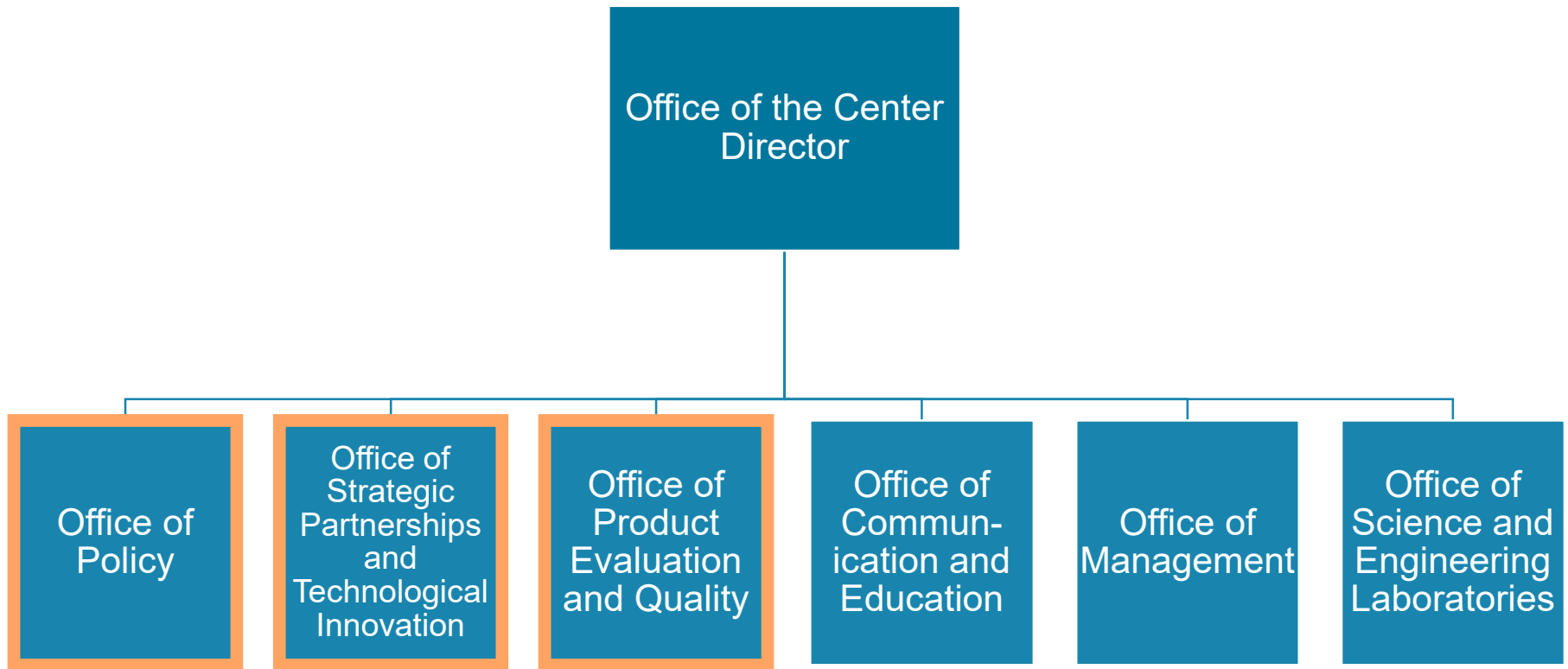
# CDRH Reorganization

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- Initiated March 18, 2019
  - Expected completion: September 30, 2019
- Adopts a total product lifecycle (TPLC) approach
- Establishes a “Super Office”: Office of Product Evaluation and Quality (OPEQ)
- Two additional new offices created:
  - Office of Policy
  - Office of Strategic Partnerships and Technological Innovation



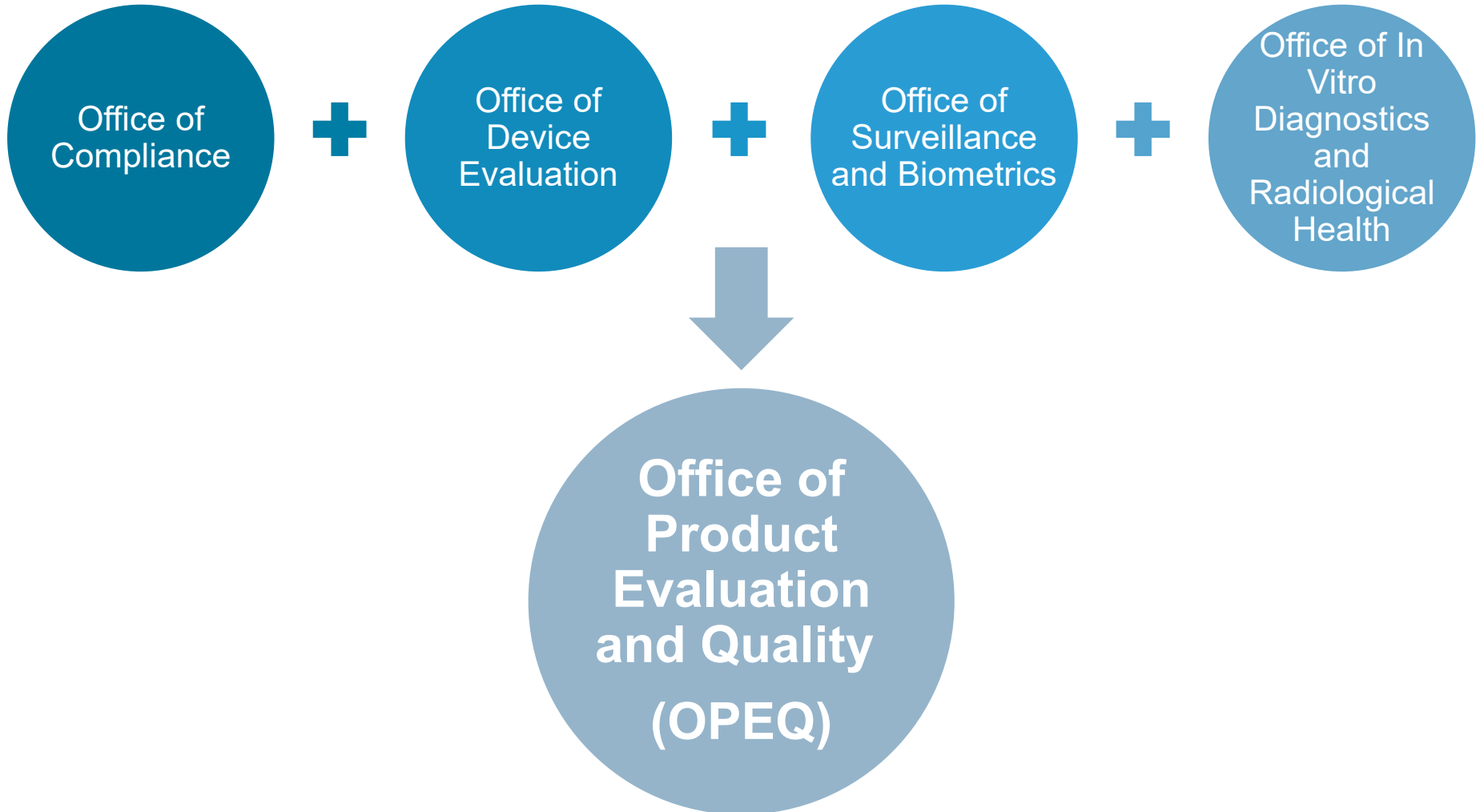
# CDRH Reorganization



New office

# OPEQ

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# Office of Product Evaluation and Quality (OPEQ)

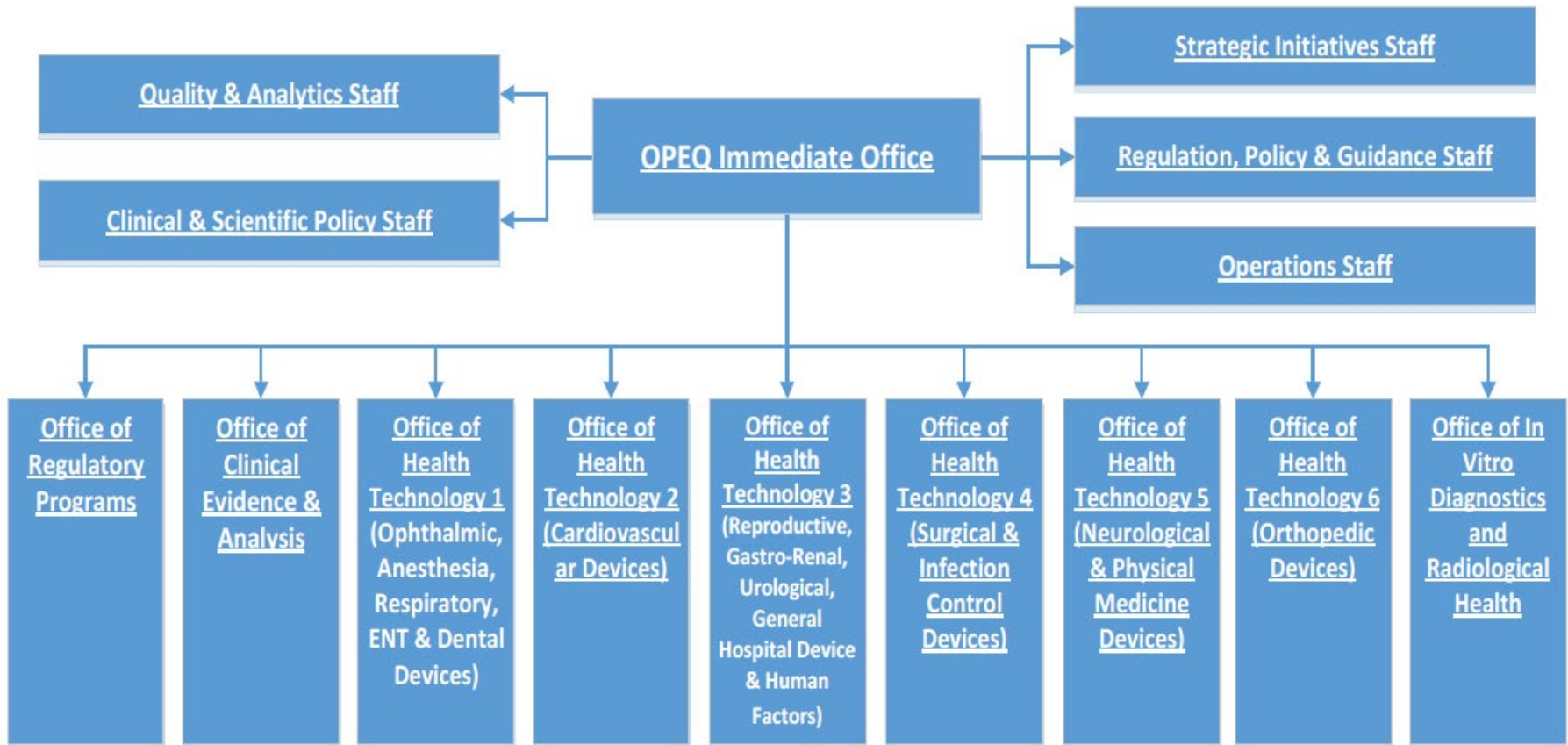
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- Director: Bill Maisel
- Combines OC, ODE, OSB, and OIR
- Nine sub-offices
  - Seven offices specific to device types
  - Two support offices
    - Office of Regulatory Programs
      - Capt. Sean Boyd
    - Office of Clinical Evidence and Analysis
      - Owen Faris



# OPEQ Structure







# CDRH Reorganization: What to Expect

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## Better internal connections within CDRH

- Eliminates silos
- Streamlines decision making
- More efficient premarket and compliance reviews
- “Cradle to Grave” concept to manage issues as they arise

## Improved manager-to-staff ratio

- Better oversight

For now, continue to interact with the same people



# CDRH Guidance Agenda, FY 2019













# FY 2019 Guidance Agenda: Final Guidance, A-List



Guidance Topic	Issued?
Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions	Not yet
Unique Device Identification: Policy Regarding Compliance Dates for Class I and Unclassified Devices and Direct Marking of Inventory	Nov. 5, 2018
Breakthrough Devices Program	Dec. 18, 2018
Safety and Performance Based Pathway (previously, Abbreviated 510(k) Program)	Feb. 1, 2019
The Least Burdensome Provisions: Concept and Principles	Feb. 5, 2019
Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act	Not yet
Clinical and Patient Decision Support Software	Not yet
Multiple Function Device Products: Policy and Considerations	Not yet
Humanitarian Device Exemption (HDE) Program	Not yet
Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program	Not yet
The Special 510(k) Program	Not yet

# FY 2019 Guidance Agenda: Draft Guidance, A-List



Draft Guidance Topic	Issued?
Content of Premarket Submissions for Cybersecurity of Medical Devices of Moderate and Major Level of Concern	Oct. 18, 2018 
Surgical Staplers and Staples – Labeling Recommendations	Not yet 
Nonbinding Feedback After Certain FDA Inspections of Device Establishments	Feb. 19, 2019 
Select Updates for Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices	Nov. 29, 2018 
Recommendations for Dual 510(k) and Clinical Laboratory Improvement Amendments Waiver by Application Studies	Nov. 29, 2018 
Computer Software Assurance for Manufacturing, Operations, and Quality System Software	Not yet 
Patient Engagement in Clinical Trials	Not yet 
Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices	Not yet 
Lifecycle Regulatory Requirements of Medical Device Servicing (Device Servicer vs Remanufacturer)	Not yet 
Guidance on an Accreditation Scheme for Conformity Assessment of Medical Devices to FDA-Recognized Consensus Standards (ASCA)	Not yet 

# FY 2019 Guidance Agenda: B-List



## Final Guidance Topics

Utilizing Animal Studies to Evaluate Organ Preservation Devices	Not yet	✗
Unique Device Identification: Convenience Kits	Not yet	✗
Medical X-Ray Imaging Devices Conformance with IEC Standards	Not yet	✗
Replacement Reagent and Instrument Family Policy for In Vitro Diagnostic Devices	Not yet	✗
Unique Device Identification System: Form and Content of the Unique Device Identifier (UDI)	Not yet	✗

## Draft Guidance Topics

Implanted Brain-Computer Interface (BCI) Devices for Patients with Paralysis or Amputation – Non-clinical Testing and Clinical Considerations	Feb. 25, 2019	✓
Continuous Ventilators - Premarket Notification (510(k)) Submissions	Not yet	✗



# 2019 Guidance: What to Expect

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Roughly half way through the FY 2019 Guidance Agenda

- Only 9 of 28 have been issued
- Expect FDA to issue many of the remaining A-list guidances, e.g.,
  - Clinical and Patient Decision Support (final)
  - Multiple function devices (final)
  - Special 510(k) program (final)
  - Premarket submission considerations for software in a medical device (draft)

Guidance not on the agenda, but expected:

- Inspections processes and standards (draft) – pub. March 19, 2019
- De Novo refuse to accept policy (final)
- First examples of product-specific safety and performance based pathway guidances (draft)
- Postmarket Safety Reporting for Combination Products (final)

# FDARA Update





# Recap: FDA Reauthorization Act of 2017

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- Effective August 18, 2017
- User fee reauthorizations, including MDUFA
- Beneficial provisions for device firms

Risk-based  
inspection  
schedule

Uniform  
inspection  
processes and  
standards

Feedback on  
FDA-483  
responses

Improvements to  
CFG issuance

Medical device  
accessory  
regulatory  
pathway

New guidance  
documents



# Status of Select Actions Required by FDARA



Guidance Topic	
Report on FDA website re: servicing of devices	Released May 15, 2018 ✓
Meeting on pediatric device development	Held Aug. 13-14, 2018 ✓
Draft guidance on CFGs, explanation of denials and review process	Issued Aug. 17, 2018 ✓
Draft guidance on inspection process, timeframes, and feedback	Issued February 19 and March 29, 2019 ✓
Annual reports on pre-approval inspections	Issued reports for CY 2017, CY 2018 ✓
Draft guidance on pilot program for Accreditation Scheme for Conformity Assessments	Pilot program announced, on CDRH FY 2019 A-List ✓
Final guidance on process for requesting review of CFG denials	Not yet; due Nov. 15, 2019 ✓

# Recent FDARA Draft Guidance: 483 Feedback

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## *Nonbinding Feedback after Certain FDA Inspections of Device Establishments*

- Issued Feb. 19, 2019
  - Comments until Apr. 22, 2019, [FDA-2018-D-4711](#)
- Process for requesting feedback on 483 corrective action plan:
  - Written request
  - No later than 15 business days after 483
  - Same submission as 483 response, but **distinct documents**

# Recent FDARA Draft Guidance: 483 Feedback

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## Request must establish applicability of one of three criteria:

1. Likely to result in the release of a violative product that may cause death or serious injury
2. Has resulted in, or would likely result in, the production of nonconforming, violative, and/or defective finished devices
3. An emerging safety issue that, if unresolved, is likely to result in release of devices that are likely to cause death or serious injury

# Device Inspections Processes and Standards

## Draft Guidance

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- Issued March 29, 2019; Comment period open 60 days
- Uniform processes and standards for routine inspections
  - Pre-announcement of inspection
    - No less than 5 days in advance for domestic inspections
    - Longer for foreign inspections due to country clearances
    - Will advise if the inspection is comprehensive, abbreviated, PAI
  - Typical inspection will last 3 – 6 consecutive business days
    - May need to extend due to complexity of operations, post market follow-up to complaint, recalls, etc.
    - Expected working hours and records to be requested
  - FDA retains the right to conduct unannounced “for-cause” inspections
- As time and circumstances permit, investigators *should* discuss all observations with management as they are observed, or on a daily basis, to minimize errors and misunderstandings
- Communications may be recorded by either FDA or the firm, if there is advance notice and mutual consent

# What to Expect: “Servicing” Devices



- FDARA-required report on servicing of devices
  - Issued May 15, 2018
  - Declined to impose additional regulatory requirements on servicing
    - High-quality, safe, and effective servicing of devices
    - Third-party servicers are critical to the functioning of the healthcare system
    - No evidence of a widespread public health concern
- But report distinguished servicing from remanufacturing
  - Guidance coming this year on the difference, and the regulatory requirements
    - Open public meeting held December 10-11, 2018
      - Still seeking public comment

# Overview of Recent Premarket Polices and Pilots

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# FY 2019: Pre-Market Program Changes

## Policies/Programs

- Quality in 510(k) Review Program Pilot (Sept. 6, 2018)
- Special 510(k) Pilot (Oct 1, 2019)
- Least Burdensome “Flag” for 510(k)s (Mar. 4, 2019)

## Guidances

- Cybersecurity Content in Premarket Submissions (Draft, Oct. 18, 2018)
- Manufacturing Site Change Supplements (Final, Dec. 17, 2018)
- Breakthrough Devices Program (Final, Dec. 18, 2019)
- Safety and Performance Based Pathway (Final, Feb. 2, 2019)
- Premarket Pathways for Combination Products (Draft, Feb. 2019)
- Least Burdensome Provisions (Final, Feb. 5, 2019)
- Refuse to Accept Policy for 510(k)s (Final, Feb. 21, 2019)
- Refuse to Accept Policy for PMAs (Final, Feb. 21, 2019)

## Proposed Rule

- De Novo (Dec. 7, 2018)



# Recent 510(k) Program Changes

## RTA Addendum

- Notifies sponsor of potential issues at RTA stage

## 10-Day Call

- Optional, 30-minute teleconference within 10 days of receipt of AI letter to obtain clarification about AI requests

## First Round NSE

- Permits resolution of “high-level” NSE issues without putting submission on hold

## Least Burdensome Flag

- Sponsor identifies AI requests that are not least burdensome and proposes alternatives

## Safety and Performance Based Pathway

- Expands abbreviated 510(k) program; relies on recognized standards

## Quality in 510(k) Review

- Uses eSubmitter to shorten FDA review by 30 days

## Special 510(k) Pilot

- Expands types of changes that qualify for Special 510(k)s





# Safety and Performance Based Pathway

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- Final guidance issued Feb. 1, 2019 (draft Apr. 12, 2018)
- Demonstrate device meets FDA-identified performance criteria and expectations
  - Optional program; traditional 510(k) substantial equivalence paradigm still available
  - May reference international consensus standards
- **Eligibility limited to FDA-identified device types**
  - List of eligible procodes to be maintained on FDA's website
  - Performance criteria to be identified in guidance documents
    - FDA working on initial draft guidances now
- Opportunity for international harmonization



# Quality in 510(k) Review Pilot Program

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- Pilot launched Sept. 6, 2018
- Uses FDA's eSubmitter free software to prepare and format 510(k) submission
  - Eliminates RTA phase
  - Uses interactive review; submissions not put on hold for AI requests
  - Goal: decision within 60 days
- **Eligibility limited to certain procodes**
  - [Listed on FDA's website](#)
- Coming soon: using eSTAR, new program
  - Uses IMDRF harmonized table of contents



# Special 510(k) Pilot Program

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- Pilot [launched](#) Oct. 1, 2018
- Aims to expand types of device changes eligible for Special 510(k) submissions
- **Eligibility factors:**
  1. Special 510(k) is submitted by the existing device's mfr.;
  2. Performance data are unnecessary OR well-established methods are available to evaluate the change; and
  3. Performance data can be reviewed in a summary or risk analysis format
- Special 510(k) content/process remains unchanged
- Goal: process submissions within 30 days
  - Uses interactive review
- Ineligible submissions will be converted to traditional 510(k)s



# Breakthrough Devices Program

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- Final guidance [issued](#) Dec. 18, 2018 (draft Oct. 25, 2017)
  - Previously called Expedited Access
- **Eligibility:** PMA, 510(k), and De Novo devices that:
  1. Provide more effective treatment/diagnosis of life-threatening or irreversibly debilitating disease/condition and
  2. Either
    - Breakthrough technology,
    - No approved/cleared alternatives,
    - Significant advantages over existing alternatives, or
    - Availability is in patients' best interests
- Advantages
  - Interactive and timely communication
  - Flexible clinical study design
  - Priority review of submissions
  - Potential reliance on post-market data, post-approval inspections



# De Novo Proposed Rule

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- Issued: Dec. 7, 2018
  - Comments closed: Mar. 7, 2019
- Formalizes what FDA is already doing under guidance
  - Not meant to make major changes to review process
  - But
    - Extends PAIs to De Novo submissions, and
    - Requires submission of labeling and advertisements
- **Retains current eligibility**: Class I or II devices without a legally marketed predicate

# Case for Quality

## Voluntary Improvement Program (CfQ VIP)

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- Previously called Voluntary Medical Device Manufacturing and Product Quality Pilot Program
  - [Pilot program](#): Jan. 1, 2018 to Dec. 31, 2018
  - Leverages third-party Capability Maturity Model Integration (CMMI) appraisal
- Benefits:
  - No routine inspections
  - Waiver of most PAIs
  - Reduced/expedited manufacturing-related submissions
- Pilot results:
  - 18 participating firms; 32 appraisals
  - 40 routine inspections and 4 PAIs waived
  - 2.8 days: avg. time for review of change notices
  - 86% report positive impact on product quality

# Current Inspection and Enforcement Data

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# FDA Medical Device Enforcement and Quality Report (Nov. 2018)



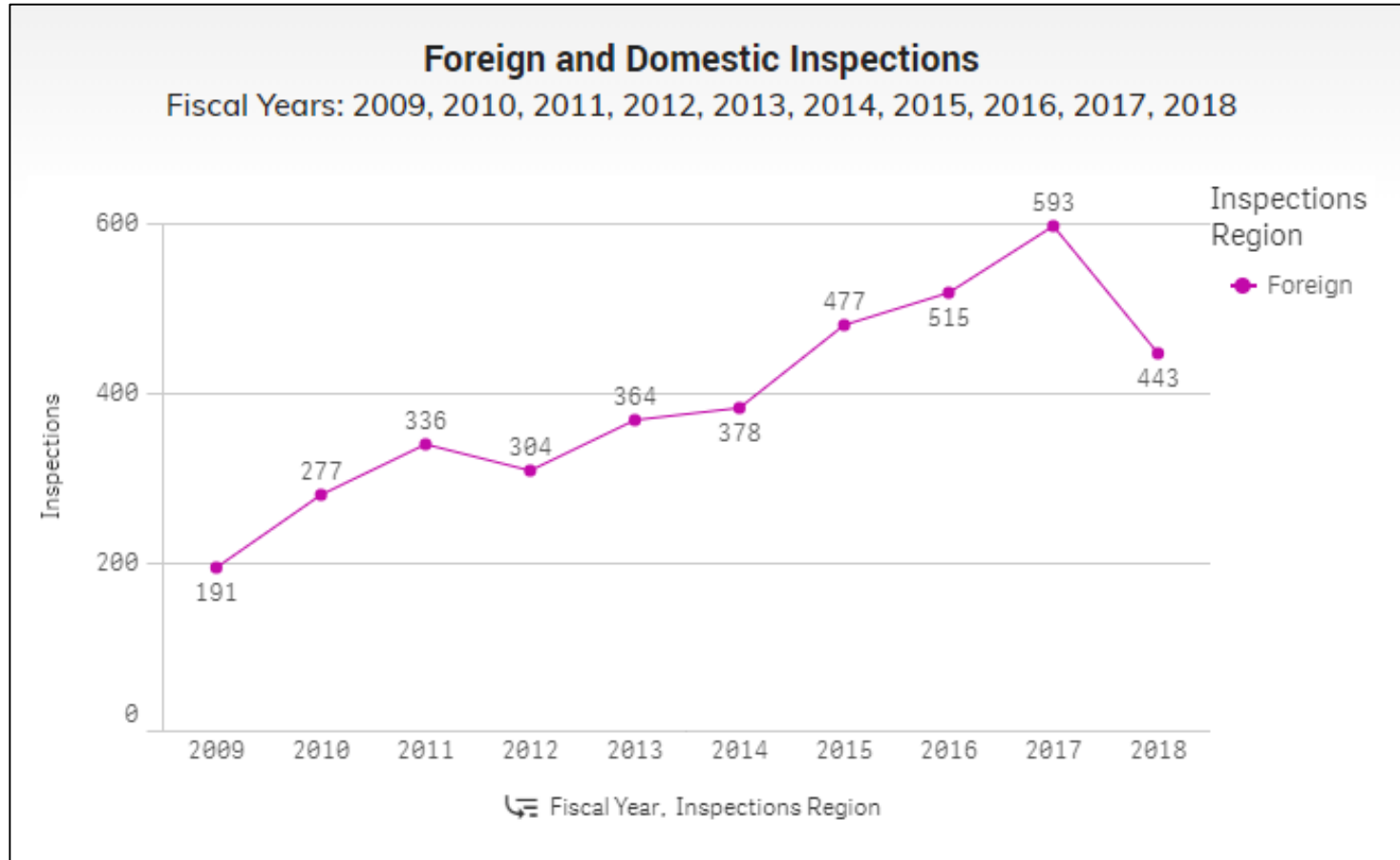
## Medical Device Enforcement and Quality Report

November 2018

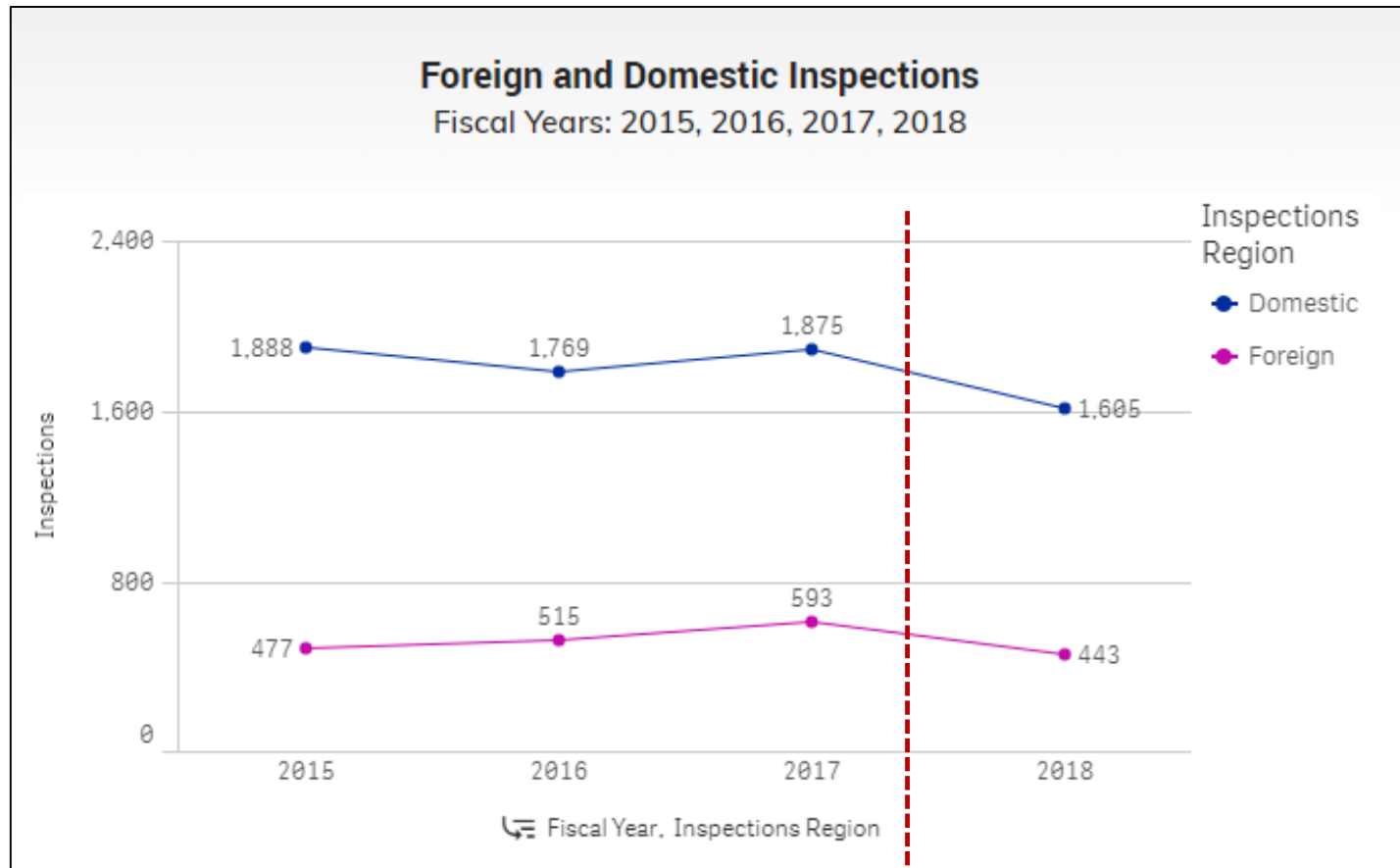
“In the past decade, the FDA has increased ...the annual number of device manufacturing establishment inspections. Inspections of medical device firms, representing a 46% increase compared to a decade earlier. In addition, the FDA has increased the number of foreign inspections during the same time period by 243%.”



# Foreign Inspections (Devices) FY 2009 – FY 2018



# Device Inspections FY 2015 to FY 2018, Before and After MDSAP



**MDSAP fully operational  
(Jan. 1, 2017)**

# FDA Medical Device Enforcement and Quality Report (Nov. 2018) (cont'd)



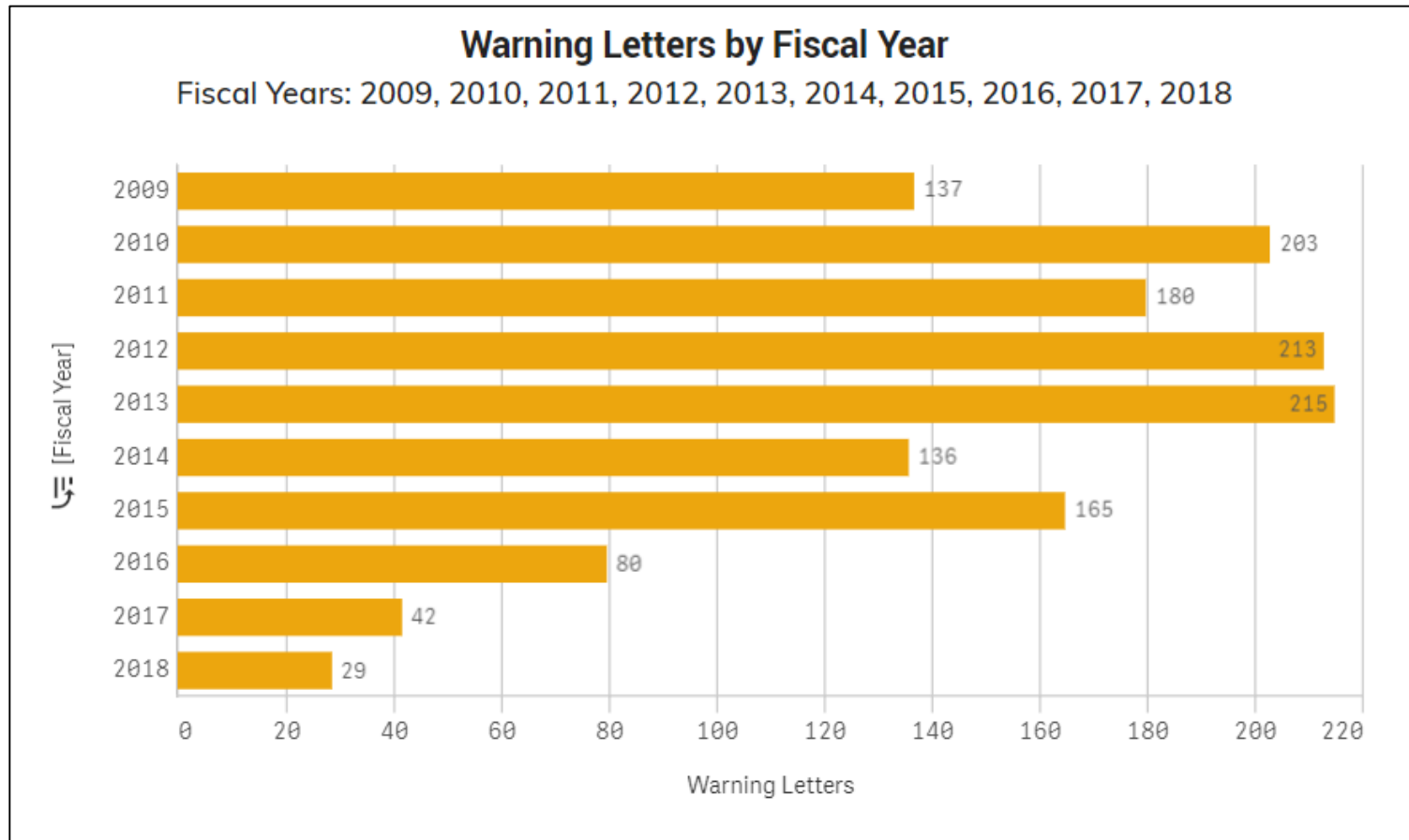
## Medical Device Enforcement and Quality Report

November 2018

“The FDA took a more aggressive approach to the issuance of Warning Letters for violative manufacturers beginning in 2008 and reaching a peak in 2012.... More recently, the FDA has been more interactive with violative firms, recognizing that, where appropriate, it can be an effective approach to achieving more timely and effective corrective action.... This more interactive approach has resulted in a decrease in the annual number of Warning Letters, with an increase in Untitled Letters, regulatory and other meetings.....”

# Warning Letters (Devices)

## FY 2009 – FY 2018





# Looking Ahead





# International Harmonization

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- QSR and ISO 13485 Harmonization
  - It's happening!
  - But conversion to 13485 will take many years
  - Notice of Proposed Rulemaking targeted this calendar year
  - Enhances global compliance and complements MDSAP
- Single Premarket Review
  - Aspirational, for now
  - Would rely on common data elements, performance expectations
  - Would use a harmonized electronic submission
  - Currently: IMDRF piloting a common regulated product submission table of contents



# Focus on Materials and Biocompatibility

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- Joint Gottlieb/Shuren [statement](#) (Mar. 15, 2019)
  - “[W]e believe the current evidence, although limited, suggests some individuals may be predisposed to develop an immune/inflammatory reaction when exposed to select materials.”
  - Cites breast implants, metals (nitinol, metal-on-metal hips), animal materials in devices
- Advisory Committee Meetings
  - Breast implants and reconstructive mesh (Mar. 25-26, 2019)
  - Materials/metals in medical devices (Fall 2019)
    - To be preceded by an FDA white paper on metal implants



# CDRH Goals that Will Continue

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## First in world approval/clearance

- Improving speed in time to approval/clearance
- Draft/final premarket guidance and pilot programs

## But continued focus on safety

- Perhaps a reaction to media reports in 2018

## International harmonization

- MDSAP
- Increased use of consensus standards (e.g., Safety and Performance Based Pathway)
- ISO 13485 adoption
- IMDRF table of contents adoption



# Thank You

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