FDANews Medical Device Quality Congress

FDA Medical Device Regulation Agenda:
Are you Prepared?
April 23, 2019

PRESENTED BY:
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Agenda

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

- *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

Office of the Center Director

Office of Policy
Office of Strategic Partnerships and Technological Innovation
Office of Product Evaluation and Quality
Office of Communication and Education
Office of Management
Office of Science and Engineering Laboratories

New office
OPEQ

Office of Compliance + Office of Device Evaluation + Office of Surveillance and Biometrics + Office of In Vitro Diagnostics and Radiological Health

Office of Product Evaluation and Quality (OPEQ)
Office of Product Evaluation and Quality (OPEQ)

- 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

Quality & Analytics Staff

Clinical & Scientific Policy Staff

OPEQ Immediate Office

Strategic Initiatives Staff

Regulation, Policy & Guidance Staff

Operations Staff

Office of Regulatory Programs

Office of Clinical Evidence & Analysis

Office of Health Technology 1 (Ophthalmic, Anesthesia, Respiratory, ENT & Dental Devices)

Office of Health Technology 2 (Cardiovascular Devices)

Office of Health Technology 3 (Reproductive, Gastro-Renal, Urological, General Hospital Device & Human Factors)

Office of Health Technology 4 (Surgical & Infection Control Devices)

Office of Health Technology 5 (Neurological & Physical Medicine Devices)

Office of Health Technology 6 (Orthopedic Devices)

Office of In Vitro Diagnostics and Radiological Health
CDRH Reorganization: What to Expect

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

<table>
<thead>
<tr>
<th>Guidance Topic</th>
<th>Issued?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions</td>
<td>Not yet</td>
</tr>
<tr>
<td>Unique Device Identification: Policy Regarding Compliance Dates for Class I and Unclassified Devices and Direct Marking of Inventory</td>
<td>Nov. 5, 2018 ✓</td>
</tr>
<tr>
<td>Breakthrough Devices Program</td>
<td>Dec. 18, 2018 ✓</td>
</tr>
<tr>
<td>Safety and Performance Based Pathway (previously, Abbreviated 510(k) Program)</td>
<td>Feb. 1, 2019 ✓</td>
</tr>
<tr>
<td>The Least Burdensome Provisions: Concept and Principles</td>
<td>Feb. 5, 2019 ✓</td>
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<tr>
<td>Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act</td>
<td>Not yet</td>
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<tr>
<td>Clinical and Patient Decision Support Software</td>
<td>Not yet</td>
</tr>
<tr>
<td>Multiple Function Device Products: Policy and Considerations</td>
<td>Not yet</td>
</tr>
<tr>
<td>Humanitarian Device Exemption (HDE) Program</td>
<td>Not yet</td>
</tr>
<tr>
<td>Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program</td>
<td>Not yet</td>
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<tr>
<td>The Special 510(k) Program</td>
<td>Not yet</td>
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<table>
<thead>
<tr>
<th>Draft Guidance Topic</th>
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<tbody>
<tr>
<td>Content of Premarket Submissions for Cybersecurity of Medical Devices of Moderate and Major Level of Concern</td>
<td>Oct. 18, 2018</td>
</tr>
<tr>
<td>Surgical Staplers and Staples – Labeling Recommendations</td>
<td>Not yet</td>
</tr>
<tr>
<td>Nonbinding Feedback After Certain FDA Inspections of Device Establishments</td>
<td>Feb. 19, 2019</td>
</tr>
<tr>
<td>Select Updates for Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices</td>
<td>Nov. 29, 2018</td>
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<tr>
<td>Recommendations for Dual 510(k) and Clinical Laboratory Improvement Amendments Waiver by Application Studies</td>
<td>Nov. 29, 2018</td>
</tr>
<tr>
<td>Computer Software Assurance for Manufacturing, Operations, and Quality System Software</td>
<td>Not yet</td>
</tr>
<tr>
<td>Patient Engagement in Clinical Trials</td>
<td>Not yet</td>
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<tr>
<td>Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices</td>
<td>Not yet</td>
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<tr>
<td>Lifecycle Regulatory Requirements of Medical Device Servicing (Device Servicer vs Remanufacturer)</td>
<td>Not yet</td>
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<tr>
<td>Guidance on an Accreditation Scheme for Conformity Assessment of Medical Devices to FDA-Recognized Consensus Standards (ASCA)</td>
<td>Not yet</td>
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## FY 2019 Guidance Agenda: B-List

### Final Guidance Topics

<table>
<thead>
<tr>
<th>Topic</th>
<th>Status</th>
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<tbody>
<tr>
<td>Utilizing Animal Studies to Evaluate Organ Preservation Devices</td>
<td>Not yet</td>
</tr>
<tr>
<td>Unique Device Identification: Convenience Kits</td>
<td>Not yet</td>
</tr>
<tr>
<td>Medical X-Ray Imaging Devices Conformance with IEC Standards</td>
<td>Not yet</td>
</tr>
<tr>
<td>Replacement Reagent and Instrument Family Policy for In Vitro Diagnostic Devices</td>
<td>Not yet</td>
</tr>
<tr>
<td>Unique Device Identification System: Form and Content of the Unique Device Identifier (UDI)</td>
<td>Not yet</td>
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### Draft Guidance Topics

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

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

- 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

<table>
<thead>
<tr>
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<tr>
<td>Report on FDA website re: servicing of devices</td>
<td>Released May 15, 2018</td>
</tr>
<tr>
<td>Meeting on pediatric device development</td>
<td>Held Aug. 13-14, 2018</td>
</tr>
<tr>
<td>Draft guidance on CFGs, explanation of denials and review process</td>
<td>Issued Aug. 17, 2018</td>
</tr>
<tr>
<td>Draft guidance on inspection process, timeframes, and feedback</td>
<td>Issued February 19 and March 29, 2019</td>
</tr>
<tr>
<td>Annual reports on pre-approval inspections</td>
<td>Issued reports for CY 2017, CY 2018</td>
</tr>
<tr>
<td>Draft guidance on pilot program for Accreditation Scheme for Conformity Assessments</td>
<td>Pilot program announced, on CDRH FY 2019 A-List</td>
</tr>
<tr>
<td>Final guidance on process for requesting review of CFG denials</td>
<td>Not yet; due Nov. 15, 2019</td>
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Recent FDARA Draft Guidance: 483 Feedback

Nonbinding Feedback after Certain FDA Inspections of Device Establishments

- **Issued** Feb. 19, 2019
  - Comments until Apr. 22, 2019, [FDA-2018-D-4711](https://www.fda.gov/aboutFDA/legislation/docketcommunications/conferencecalls/ucm572430.htm)
  - 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

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

• 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
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

<table>
<thead>
<tr>
<th>Feature</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>RTA Addendum</strong></td>
<td>• Notifies sponsor of potential issues at RTA stage</td>
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<tr>
<td><strong>10-Day Call</strong></td>
<td>• Optional, 30-minute teleconference within 10 days of receipt of AI letter to obtain clarification about AI requests</td>
</tr>
<tr>
<td><strong>First Round NSE</strong></td>
<td>• Permits resolution of “high-level” NSE issues without putting submission on hold</td>
</tr>
<tr>
<td><strong>Least Burdensome Flag</strong></td>
<td>• Sponsor identifies AI requests that are not least burdensome and proposes alternatives</td>
</tr>
<tr>
<td><strong>Safety and Performance Based Pathway</strong></td>
<td>• Expands abbreviated 510(k) program; relies on recognized standards</td>
</tr>
<tr>
<td><strong>Quality in 510(k) Review</strong></td>
<td>• Uses eSubmitter to shorten FDA review by 30 days</td>
</tr>
<tr>
<td><strong>Special 510(k) Pilot</strong></td>
<td>• Expands types of changes that qualify for Special 510(k)s</td>
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Safety and Performance Based Pathway

• 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 procedures 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

• 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

• 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

- 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

• **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)

• 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
“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

**Foreign and Domestic Inspections**

Fiscal Years: 2015, 2016, 2017, 2018

- **Domestic**
  - 2015: 1,888
  - 2016: 1,769
  - 2017: 1,875
  - 2018: 1,605

- **Foreign**
  - 2015: 477
  - 2016: 515
  - 2017: 593
  - 2018: 443

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

Warning Letters by Fiscal Year


- 2009: 137
- 2010: 203
- 2011: 180
- 2012: 213
- 2013: 215
- 2014: 136
- 2015: 165
- 2016: 80
- 2017: 42
- 2018: 29

Warning Letters

0 20 40 60 80 100 120 140 160 180 200 220
Looking Ahead
International Harmonization

- 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

- 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

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