U.S. FOOD & DRUG ADMINISTRATION

Division of Orthopedic Devices Overview/Update

Orthopedic Surgical Manufacturers Association 2018 Spring Meeting

Mark N. Melkerson

Director

Division of Orthopedic Devices

Overview

1. DOD Organization and Activities
2. Guidance Updates
3. MDUFA IV
4. Compliance Activities
5. Experiential Learning Program (ELP)
6. 510(k) Review Trends
7. MR Testing Expectations

Division of Orthopedic Devices - Organization and Activities

Division of Orthopedic Devices (DOD)

Mark N. Melkerson, Director	
Deputy Director, Science and Policy ***Katherine Kavlock, Ph.D. (Acting)***	**Deputy Director, Clinical** ***Vincent Devlin, M.D.***
DOD Review Branches (Branch Chiefs)	
Joint and Fixation Devices Branch 1 ***Jesse Muir, Ph.D. (Acting Chief – New)***	**Joint and Fixation Devices Branch 2** ***Vesa Vuniqi, M.S. (Acting Chief – New)***
Anterior Spine Devices Branch ***Melissa Hall, M.S., Chief***	**Posterior Spine Devices Branch** ***Ronald Jean, Ph.D., Chief***
Restorative & Repair Devices Branch ***Larry Coyne, Ph.D., Chief***	

Division of Orthopedic Devices

Anterior Spine Devices Branch *Melissa Hall, M.S., Chief* *Brent Showalter, Ph.D. (Acting – New)*	Posterior Spine Devices Branch *Ronald Jean, Ph.D., Chief* *Colin O'Neill, M.S., SLR*
Anterolateral plates	Laminoplasty plates
Intervertebral body fusion devices	OCT Systems
Disc replacement prostheses	Pedicle screw systems
Nucleus replacement devices	Spinous process plates
Vertebral body replacement devices	Spinous process spacers
	Sacroiliac joint fixation devices

Division of Orthopedic Devices

Joint & Fixation Devices Branch 1 *Jesse Muir, Ph.D. (Acting Chief – New)* *Peter Allen, M.S., SLR*	Joint & Fixation Devices Branch 2 Vesa Vuniqi, M.S. (Acting Chief – New) Daniel Ramsey (Acting SLR – New)
Joint prostheses: • Knees • Shoulder • Elbow • Ankle • Toe	**Joint prostheses:** • Hips • Wrist • Finger
Fracture Fixation 1: • External fixators, etc. (Product codes: (JDW, HTY, KTT, HSB, NDK, JDR, JDQ, JDS, LXT)	**Fracture Fixation 2:** • Bone staples, plates, and screws (Product codes: JDR, HWC, HRS, OBT, etc.)
Orthopedic Stereotaxic, BGS	

Division of Orthopedic Devices

Restorative & Repair Devices Branch *Laurence Coyne, Ph.D., Chief* Sarah Brittain Nelson, Ph.D. (SLR – New)
Bone cements
BMPs
Bone void fillers
HA injectables
Ligaments and Tendons
Suture anchors (Product codes MAI and MBI)
Meniscal repair
Cartilage repair

Guidance Updates

Guidance Documents in Progress

- UHMWPE – The comment period closed in May 2016 and we are working on finalizing guidance.
- Technical Considerations for Additive Manufactured Devices – Final Document issues December 4, 2017
- Suture Anchors – The comment period closed in March 2017 and we are working on finalizing guidance.
- Patient Matched Guides – Feedback was received via questions issued in FR Notice. A draft guidance is working through review.

Not DOD specific:

- Deciding When to Submit at 510(k) for a Change to an Existing Device – October 17.

Use of Real World Evidence

Contains Nonbinding Recommendations

Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices

---

Guidance for Industry and Food and Drug Administration Staff

Document issued on August 31, 2017.

Draft Guidance out for comment

Expansion of the Abbreviated 510(k) Program: Demonstrating Substantial 2 Equivalence through Performance 3 Criteria -- Draft Guidance for Industry and Food and Drug Administration Staff

- This guidance provides FDA's current thinking on expanding the use of the Abbreviated 510(k) program for demonstrating substantial equivalence for premarket notification (510(k)) submissions. The intent of the guidance is to describe an optional pathway for certain, well understood device types, where a submitter would demonstrate that a new device meets FDA identified performance criteria to demonstrate that the device is as safe and effective as a legally marketed device.
- Comment period closes July 11, 2018

MDUFA IV

MDUFA IV

510(k) and PMA Program changes

- Categorization of deficiencies into Major, Minor, and Additional Consideration categories
- PMA and 510(k) performance goals now based on Total Time to Decision
- No other policy or process changes occurring for the 510(k) or PMA programs.
- Guidance Document (updated): "Developing and Responding to Deficiencies in Accordance with the Least Burdensome Provisions"

MDUFA IV

Pre-submission Program Changes

- At least 3 meeting dates proposed by the sponsor, we will select from the 3 dates or propose 2 new meeting dates by day 15
- Meeting date is expected to be finalized by day 30
- Written feedback is expected to be sent by day 70 or 5 calendar days prior to the meeting
- Guidance Document (updated): "Requests for Feedback on Medical Device Submissions; The Pre-Submission Program and Meetings with Food and Drug Administration Staff"

MDUFA IV

De Novo Program Changes

- User fee associated with de novo applications
- Performance goal of making a final decision within 150 FDA days.
- Guidance Document: "FDA and Industry Actions on De Novo Classification Requests: Effect on FDA Review Clock and Goals"

Compliance Activities

Case for Quality

Why

Risk to patients from quality issues and hampered innovation in manufacturing and product development practices

- High industry focus on meeting regulatory requirements over focusing on adopting best quality practices
- Low investment in automation and digital technologies to improve manufacturing and design
- No competitive market around medical device quality

What

Collaborative effort that focuses on organizational excellence and product quality

- New ways of assessing organizational performance and focusing on quality
- Adapting regulatory oversight to increase agility, responsiveness, and enable continuous improvement
- Increasing visibility into product quality to inform purchasing decisions and market choice

What does a focus on quality mean for the medical device ecosystem?

Increased manufacturing and product confidence

Faster time to markets, better information to drive regulatory decisions, improved resource allocation

Improved patient outcomes, reduced costs, and informed users

Voluntary Medical Device Manufacturing and Product Quality Pilot

Pilot Program

- **Third-party maturity appraisal that leverages the Capability Maturity Model Integration (CMMI) framework to assess a medical device organizations capability to produce high quality devices and increase patient safety**
- **Pilot was announced on December 28, 2017 and will run from January 2, 2018 and continue through December 28, 2018**

FDA Adjustments

- **Forgo surveillance, appropriate post-approval, and risk-based inspections**
- **Manufacturing change notice submissions**
  - Streamlined submission
  - Accelerated acceptance 48 hours vs 30 days
- **Manufacturing site changes**
  - Streamlined submission
  - Accelerated approval – 1 week Target
- **Original PMA Manufacturing Section**
  - Streamlined submission
  - Forgo pre-approval inspection

These changes reduce the burden and disruption of audits, accelerate the review and approval process for changes, and shift resources to innovation and improvement.

Value across stakeholders

Value analysis considered the submissions received at FDA in 2016 and the 30-dDy Changes submitted by one location of one manufacturer, the FTEs used during previous FDA audits, and estimated monthly revenue impact of approval delays for a recently released product.

FDA

- 30-Day Notices consumed 15-22 FTEs
- Site Changes consumed 5 FTEs

*Resource estimates are based on number of 30-Days received in 2016. For the 69 30 Days it is the equivalent of 1 FTE dedicated to that site for the year.

Manufacturers

- $30M/month top line.
- $1.2M/year savings 1 facility based on optimized processes and resource allocation (69 30-Day Notices)
- FDA audit cost (10 Days) - $140K
- Limited submissions and improvements due to regulatory resources
- European product lines optimized faster/better than US.

Patients/Providers

- 11 product quality improvements at one facility to patients 60-days sooner
- Increase product improvements
- Faster implementation of corrections to safety issues

- Voluntary PMA CtQ
  - focusing on activities critical to product and process quality starting September 29, 2017
  - Aim is to have the applicant discuss device design and manufacturing process quality information with FDA early on to assist FDA in its review of the PMA manufacturing section and post-approval inspections
  - Goal to streamline the premarket approval process while assuring that a firm's quality system includes rigorous controls for features and characteristics considered critical to the safety and effectiveness of the device

FR Notice: https://www.federalregister.gov/documents/2017/09/12/2017-19258/center-for-devices-and-radiological-health-premarket-approval-application-critical-to-quality-pilot?source=govdelivery&utm_medium=email&utm_source=govdelivery

- Participation PMA CtQ
  - Submit a request for a pre-PMA q-submission meeting and follow the outline of the guidance
  - List all PMA-related sites responsible for manufacture, processing, packaging or installation
  - List all critical characteristics of the device
  - Quality System deficiencies identified in FDA's review of the manufacturing section of the applicant's PMA
  - Had an FDA inspection of the PMA-related sites conducted within the last 5 years
    - Classification NAI/VAI (not OAI or been subject to a judicial action)

Experiential Learning Program

The Experiential Learning Program (ELP) is a collaborative approach to closing the knowledge gap between emerging and innovative technology and the pre-market review of the resulting medical devices.

- Stryker Instruments covering Design and Development, Manufacturing, and Servicing, November 2
- University of Nebraska Medical Center covering Wear Testing, December 5 -7
- DePuy Synthes covering Orthopedic Registries, April 11-12

Experiential Learning Program

- Multiple Biocompatibility ELP sessions
  - American Preclinical Services in Minneapolis, MN (OCTOBER 30, 2017)
  - NAMSA in Northwood, OH (NOVEMBER 14-15, 2017) and (JANUARY 24-25, 2018)
  - WuXi AppTec in Mendota Heights, MN (JANUARY 17-18, 2018)

510(k) Review: Tips and Requests

510(k) Review Tips/Requests

- The “long history of use” statement is no longer adequate by itself to address biocompatibility;
  - If the materials and manufacturing are identical to a predicate device (e.g., in-house or contract manufacturing), this should be explicitly stated;
  - If a justification is needed to address biocompatibility, please address all elements identified in the new guidance;
- For 3-D printed devices: in-house manufacturing versus contract manufacturing

510(k) Review Tips/Requests

- Please provide redlined labeling in a 510(k) submission, and ensure that the version supplied reflects all changes since the last clearance.
- Please provide an explicit listing (e.g., table) of all changes being effected/requested in the 510(k) submission, and provide this information in a single location (e.g., Device Description, Executive Summary).
- Please ensure that you do the full battery of testing on worst-case devices in accordance with relevant guidance documents.
- Please ensure that the identified points of contact in a 510(k) submission are prepared to address interactive requests/questions, and please consider identifying all possible points of contact
- 510(k) submissions that are well-organized and easy to follow generally require fewer requests for clarification.

MR Testing Expectations

MR Safety Labeling

- Not evaluated for MR safety
  - No electrical components
  - No highly ferromagnetic materials

- MR Safe
  - Non-metallic materials only
  - Requires rationale or engineering justification (e.g., resistivity testing)
- MR Conditional
  - Requires testing to establish the conditions under which a patient with the device may be safely scanned
  - Traditional submission, not special
  - Accept bundled submissions for identical device types

MR Conditional Labeling

- **For all tests**: use bath solutions as described in standards
- **Displacement Force – ASTM F2052**
- **Torque – ASTM F2213**
- **Image Artifact – ASTM F2119**
  - Report distance from artifact edge to device
    - Not artifact area or volume
  - Report image resolution
- **Radiofrequency induced heating – ASTM F2182**
  - Computational modeling to determine worst case construct
    - Report model validation & uncertainty analysis
  - Test devices in both 1.5 T and 3.0 T systems
  - Clearly describe both local and whole-body SAR measurements
  - For devices exhibiting high temperature rises, computational model of *in vivo* use (e.g., in Duke model) may be necessary

THANK YOU

QUESTIONS?


FDA
U.S. FOOD & DRUG
ADMINISTRATION