Medical Device Safety:
FDA Considerations for New Dialysis Devices

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Division of Circulatory Support, Structural and Vascular Devices
Office of Cardiovascular Devices
Office of Product Evaluation and Quality

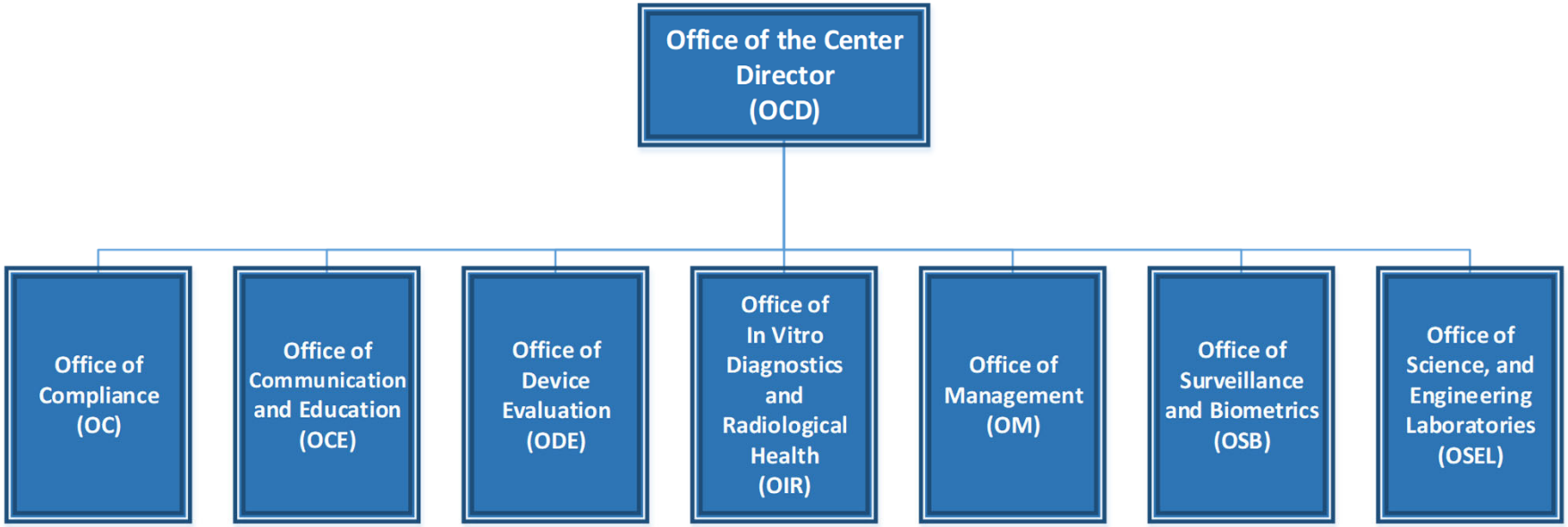
Disclosures

- I am a full time employee of the US FDA
- I have no commercial conflicts
- When I don’t cite policy or regulations, any opinions expressed are my own

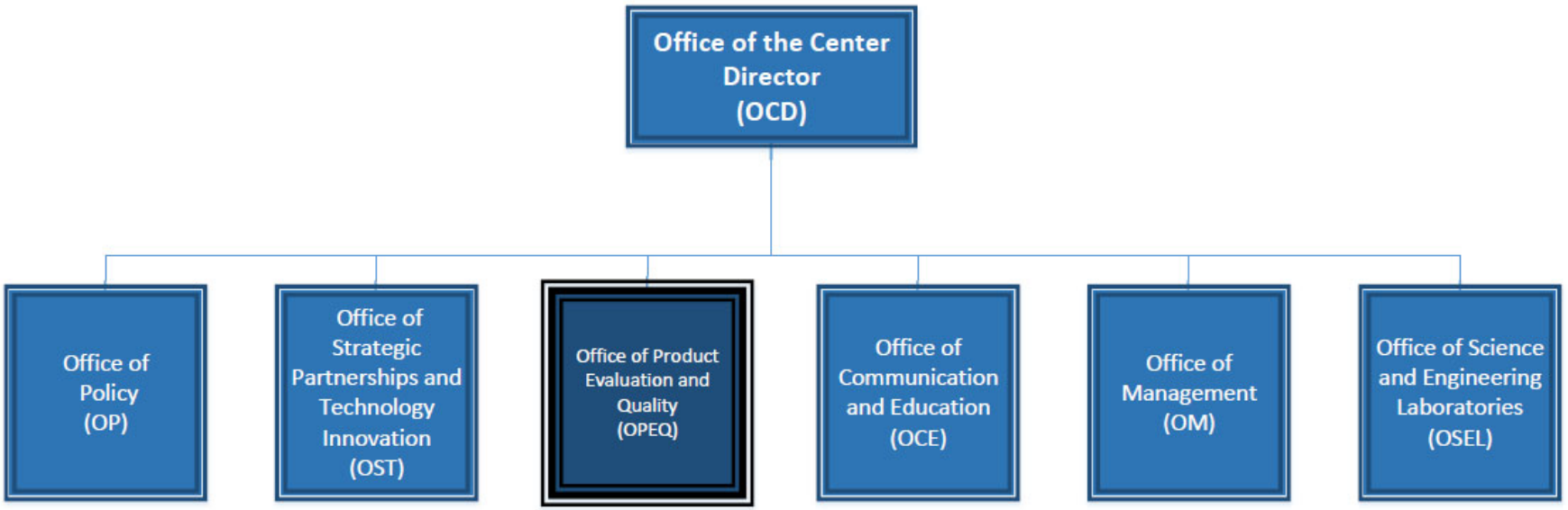
Center for Devices and Radiological Health Reorganization

- CDRH implemented a new organizational structure on May 1st, 2019.
- CDRH reorganization includes adopting a TPLC model and other efforts to streamline and improve efficiency
- Each device team has responsibility for products oversight from the premarket review phase to post market surveillance.

Prior CDRH Structure



CDRH Structure After Reorg Implementation



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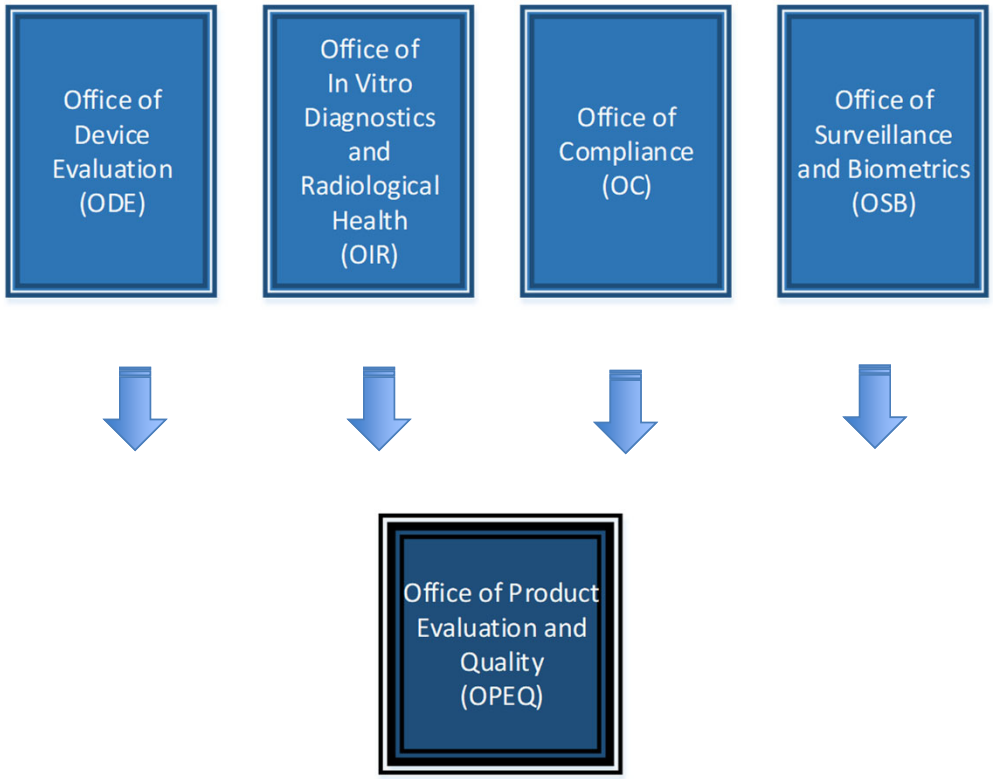

OC, ODE, OIR and OSB will reorganize into one Super Office (OPEQ)

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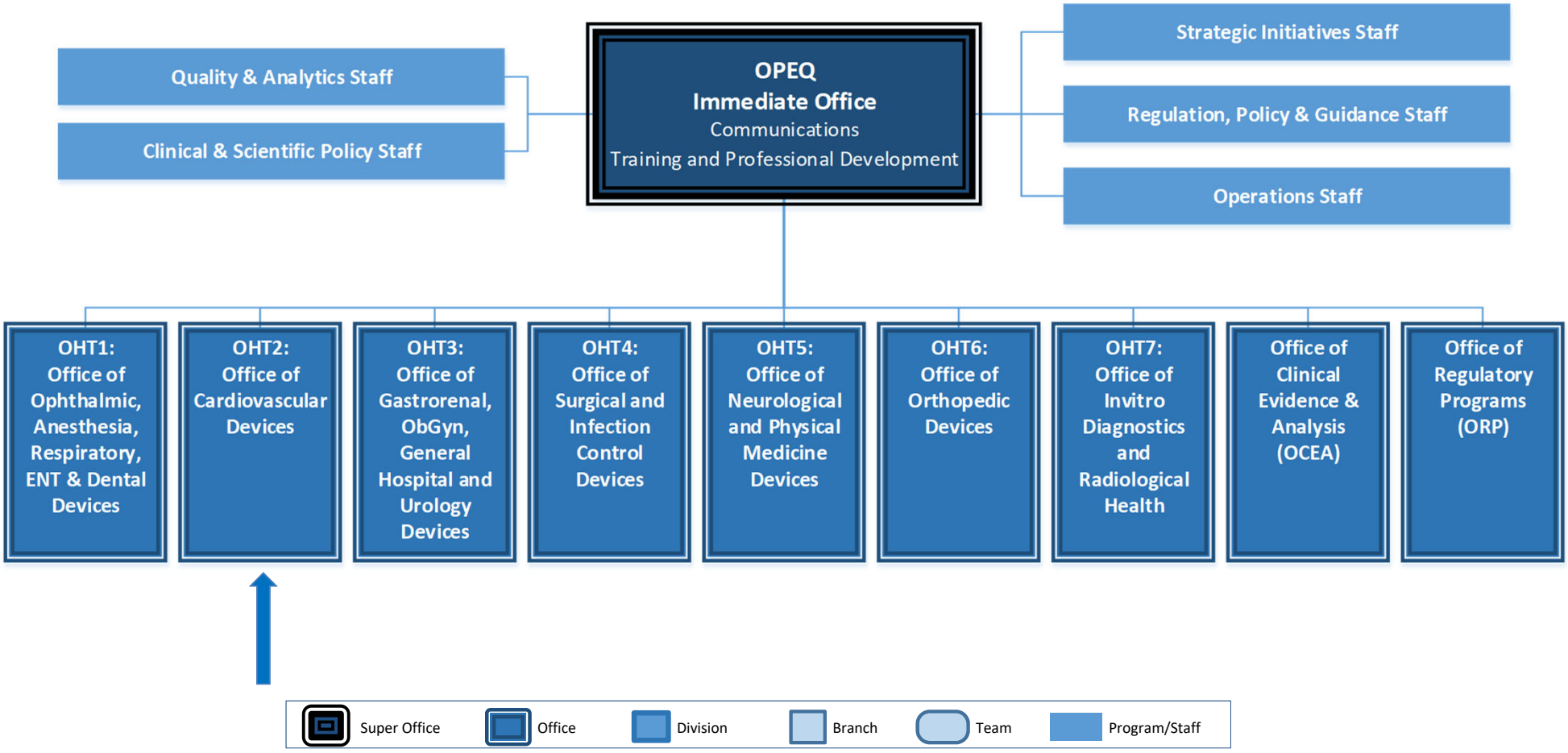


Device Classification

- Based on device description and intended use
- Class I, II, or III based on increasing degrees of risk

Classes of Medical Devices

Class	Risk	Controls	Submission
I	Lowest	General	• Exempt* • 510(k)
II	Moderate	General and Special (if available)	• 510(k)* • Exempt
III	Highest	General and PMA	• PMA

*** Most Common Submission Type for Class**

Investigational Device Exemption (IDE)

- Clinical research on investigational devices
- Collect safety and effectiveness data for future marketing application
- Requires approval by Institutional Review Board
- Protect human patients

De Novo

- Marketing process for **novel** devices
- Device has no existing classification regulation
- The pathway by which the two devices intended to create percutaneous AVF were approved in 2018

Contains Nonbinding Recommendations

Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions

Guidance for Industry and Food and Drug Administration Staff

Document issued on December 27, 2016.

The draft of this document was issued on June 16, 2016

For questions about this document regarding CDRH-regulated devices, contact the Office of Compliance at 301-796-5900.

FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DEVICES & RADIOLOGICAL HEALTH

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

[Risk Benefit Guidance]

Medical Device Benefits

- Type of benefit(s)
- Magnitude of benefit(s)
- Likelihood of patients experiencing benefit(s)
- Duration of effects
- Patient Perspective
- Benefits for providers / caregivers
- Unmet need

Risk Benefit Guidance for Medical Devices

Medical Device Risks

- **Severity of harm?**
  - **Device related deaths and serious injuries**
  - **Device related non-serious adverse events**
  - **Events with out harm**
- **Likelihood of harm?**
- **Duration of exposure to harm?**
- **Patient tolerance to harm?**

Risk Benefit Guidance for Medical Devices

Post Market Assurance

Section 522 of the Federal Food, Drug and Cosmetic Act (the act) gives FDA the authority to require a manufacturer to conduct postmarket surveillance of a class II or class III device that meets any of the following criteria:

- its failure would be reasonably likely to have serious adverse health consequences;
- it is expected to have significant use in pediatric populations;
- it is intended to be implanted in the body for more than one year; or
- it is intended to be a life-sustaining or life-supporting device used outside a device user facility

Medical Device Reporting

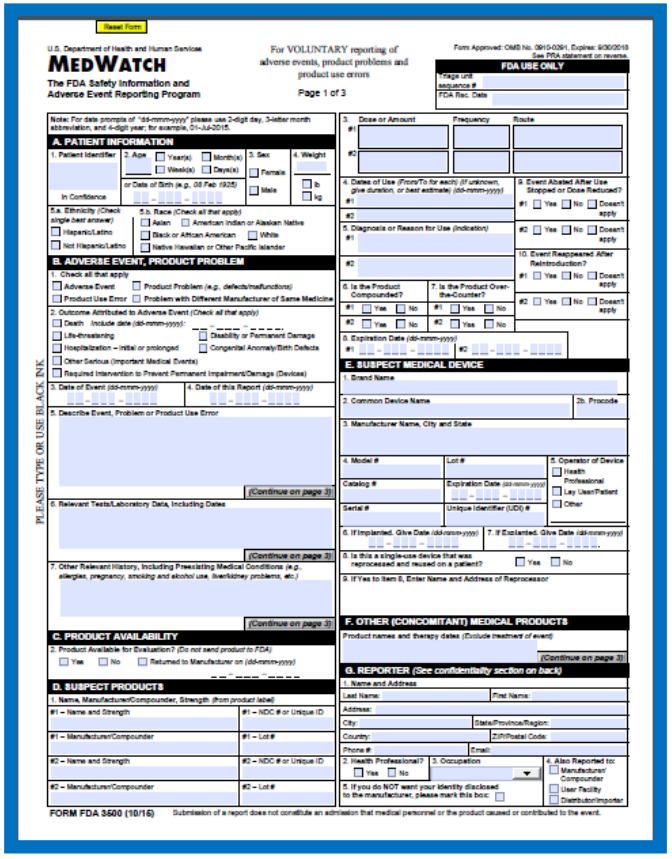
Who?

- **MANDATORY: 21 CFR 803**
  - **Manufacturers**
  - **Importers**
  - **Health Care Facilities**
- **VOLUNTARY**
  - **Health Care Providers**
  - **Consumers**

What?

- **Therapeutic Failures**
- **Product Quality Issues**
- **Serious Adverse Events (SAEs)**
  - **Death**
  - **Life threatening**
  - **Disability / Hospitalization**
  - **Requiring intervention**
  - **Congenital anomalies**

MedWatch Voluntary Reporting



U.S. Department of Health and Human Services

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

For VOLUNTARY reporting of adverse events, product problems and product use errors

Page 1 of 3

FDA USE ONLY

A. PATIENT INFORMATION

B. ADVERSE EVENT, PRODUCT PROBLEM

C. PRODUCT AVAILABILITY

D. SUSPECT PRODUCTS

E. SUSPECT MEDICAL DEVICE

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

G. REPORTER (See confidentiality section on back)

PLEASE TYPE OR USE BLACK INK

FORM FDA 3500 (10/16)

Download FDA Form 3500

Web based report form

1-800-FDA-1088: Phone

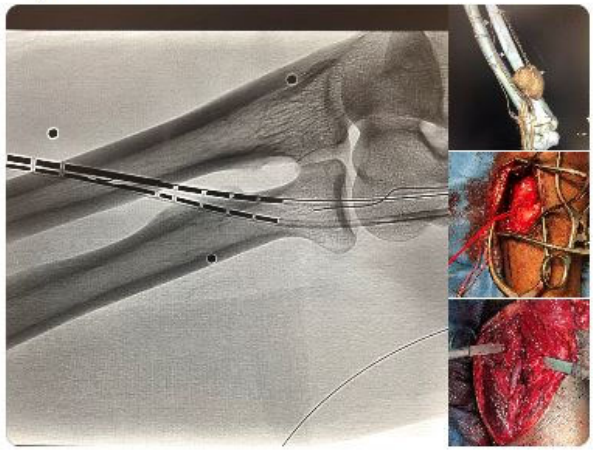
1-800-FDA-0178: FAX

Form 3500 B for Consumers

Graeme McFarland
@gemcfarland12

Follow

Large ulnar a. psa after perc AVF creation. Difficult anatomic location to access w/o muscle transection and ultimately required a bypass. Not clear on the location choice? Brachial v. was coiled and primary outflow vein was the basilic which would still need superficialization.



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Graeme McFarland @gemcfarland12 · Mar 12
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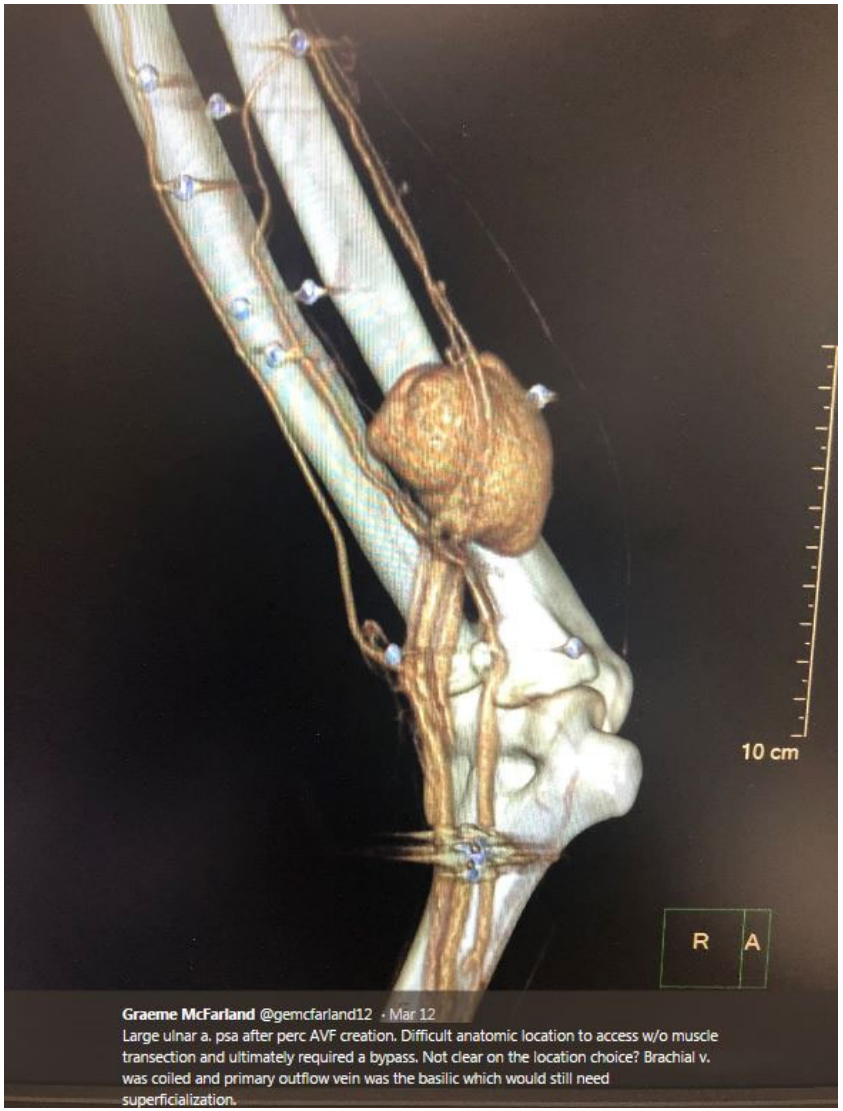

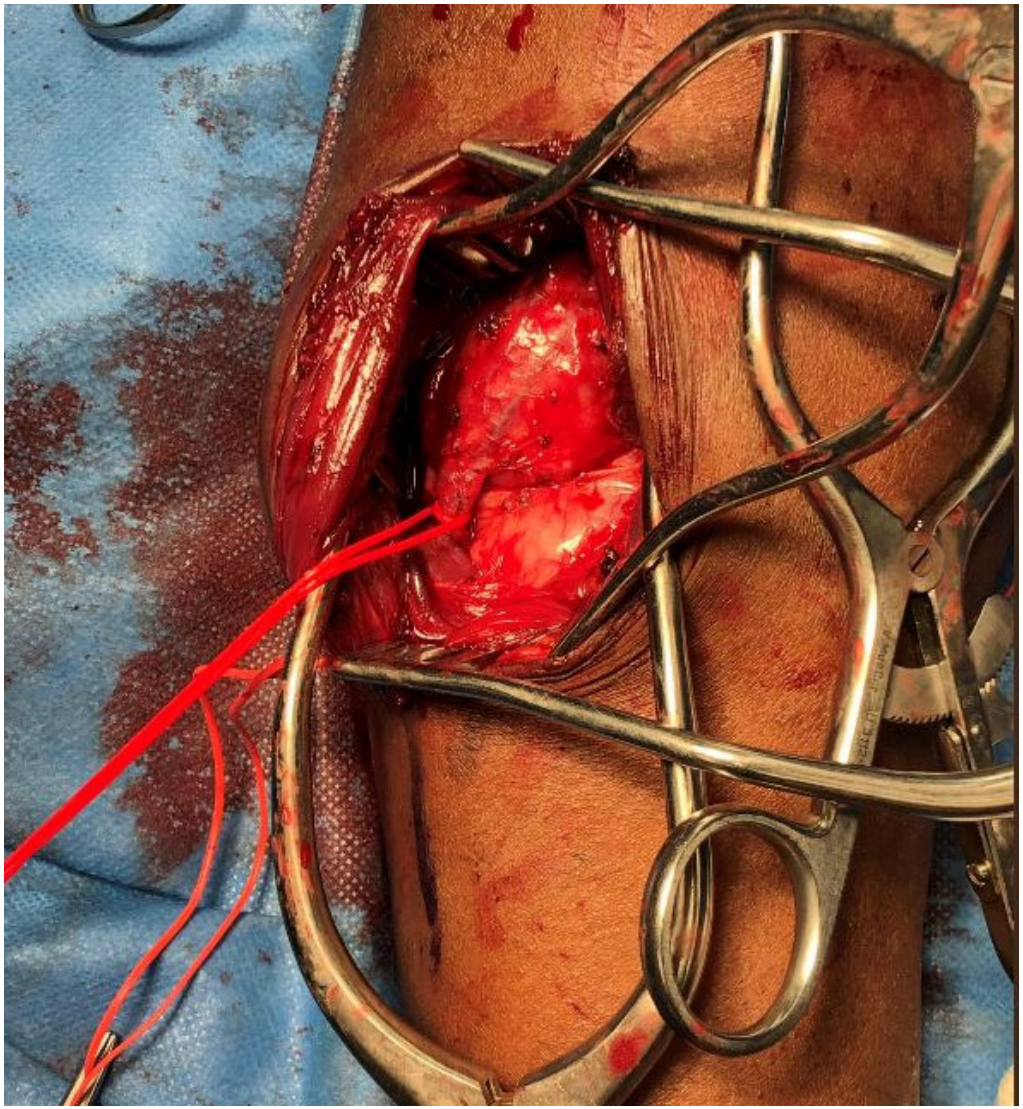

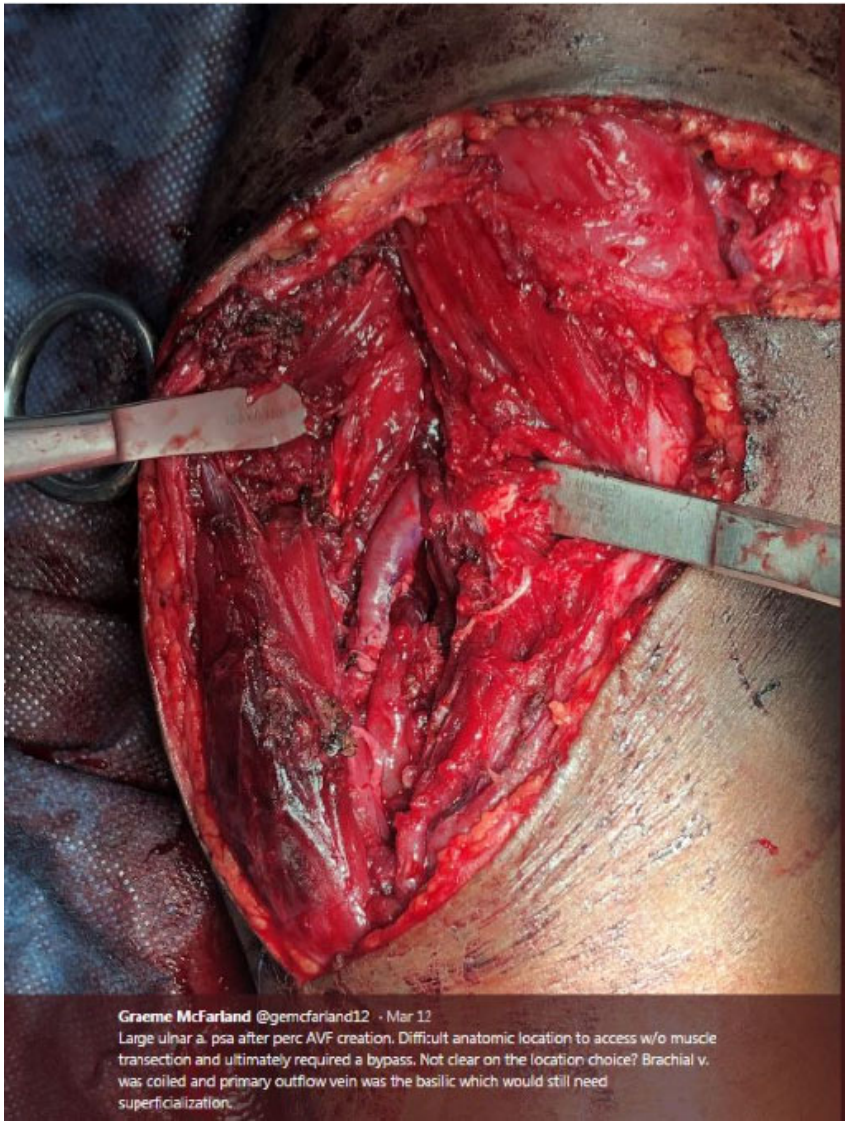
Graeme McFarland @gemcfarland12 · Mar 12
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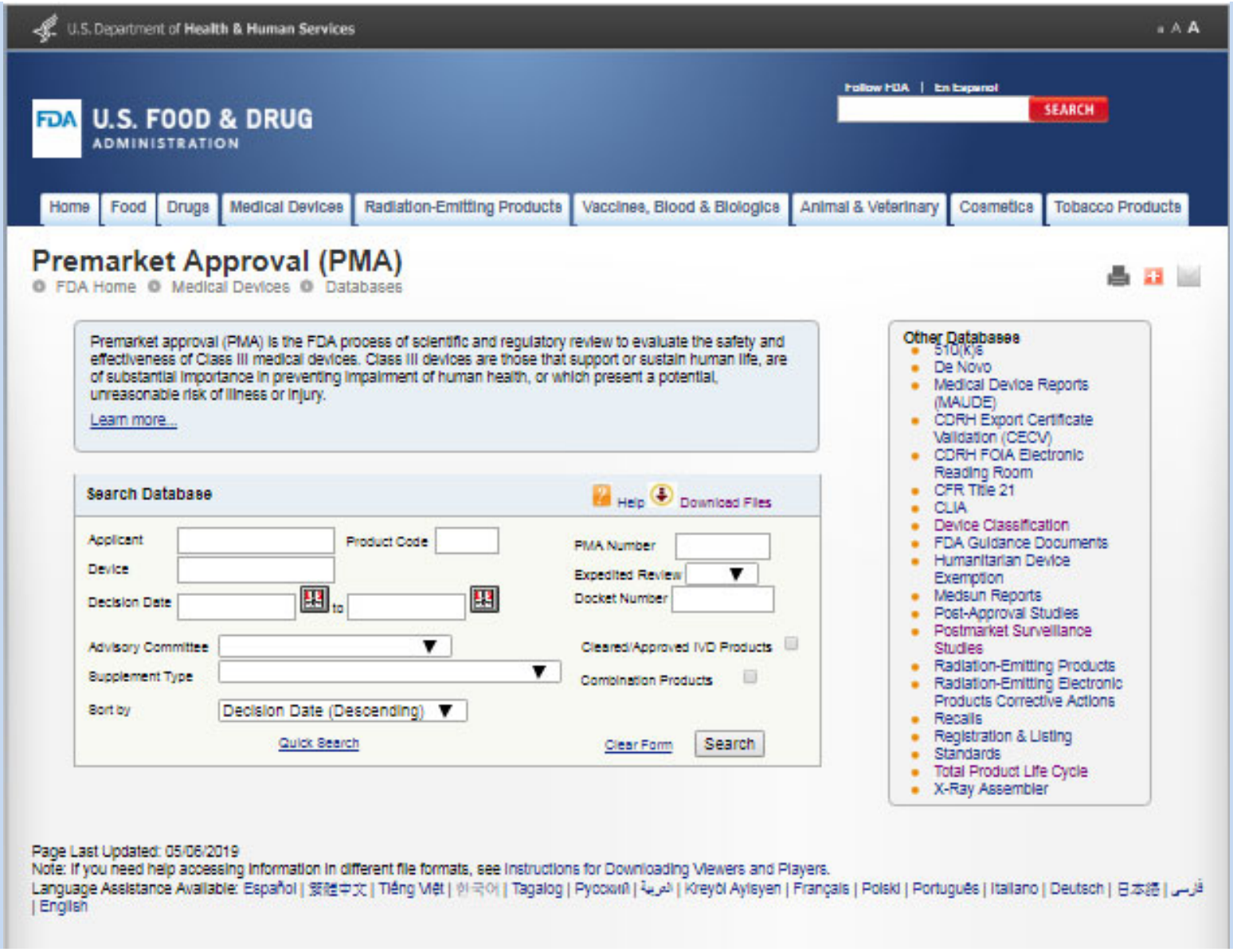
Your Role as a Clinician in Assuring Medical Device Safety

- Obtain appropriate training on novel devices

- Know your devices!
  - Read the full pivotal study reports
  - Stay Abreast of the PAS studies
  - Scrutinize the SSED for the devices you utilize

Summary of Safety and Effectiveness Data

- The SSED is an FDA document that summarizes the key content of the PMA, such as the Device Description, Preclinical Evidence, and Clinical Evidence, as well as FDA's analysis of the scientific evidence that served as the basis for FDA's decision regarding the reasonable assurance of the safety and effectiveness of the device.
- SSEDs are accessible via the FDA PMA database:
  https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm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Premarket Approval (PMA)
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Premarket approval (PMA) is the FDA process of scientific and regulatory review to evaluate the safety and effectiveness of Class III medical devices. Class III devices are those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury.
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Note: This medical device record is a PMA supplement. A supplement may have changed the device description/function or indication from that approved in the original PMA. Be sure to look at the original PMA record for more information.

Device	Covera™ Vascular Covered Stent
Classification Name	System, Endovascular Graft, Arteriovenous (Av) Dialysis Access Circuit Stenosis Treatment
Generic Name	System, Endovascular Graft, Arteriovenous (Av) Dialysis Access Circuit Stenosis Treatment
Applicant	C.R. Bard, Inc 1625 W. 3rd Street Tempe, AZ 85526
PMA Number	P170042
Supplement Number	S002
Date Received	09/04/2018
Decision Date	03/01/2019
Product Code	PFV [Registered Establishments With PFV]
Docket Number	19M-0995
Notice Date	03/07/2019
Advisory Committee	Cardiovascular
Clinical Trials	NCT02649946
Supplement Type	Panel Track
Supplement Reason	Labeling Change - Indications/Instructions/Shelf Life/Tradename
Expedited Review Granted?	No
Combination Product	No

Approval Order Statement

Approval of the COVERA Vascular Covered Stent. The device is indicated for use in hemodialysis patients for the treatment of stenoses in the venous outflow of an arterio-venous fistula and at the venous anastomosis of an ePTFE or other synthetic AV graft.

Approval Order

Approval Order

Summary

Summary Of Safety And Effectiveness

Labeling

Labeling

Labeling Part 2

Post-Approval Study Show Report Schedule And Study Progress

XII. CONCLUSIONS DRAWN FROM CLINICAL STUDY

A. Effectiveness Conclusions

To demonstrate clinically acceptable effectiveness, the primary effectiveness endpoint was evaluated against the rate of Target Lesion Primary Patency (TLPP) at 6 months for standard PTA alone. TLPP at 6 months post-index procedure was evaluated using the Kaplan-Meier analysis and results were 78.7% in the COVERA™ group and 47.9% in the PTA group. The results demonstrated that, with respect to TLPP, the COVERA™ Vascular Covered Stent was superior to the PTA control ($p < 0.001$) for treatment of stenoses in the venous outflow of patients dialyzing with an arteriovenous fistula. The key secondary effectiveness endpoint of TLPP at 12 months was also met. At 12 months, TLPP was 57.5% for COVERA™ treated subjects versus 21.2% in the PTA group.

The significant benefit in TLPP did not carry over to Access Circuit Primary Patency (ACPP). At 6 months, ACPP was 50.7% for COVERA™ treated subjects versus 43.8% in the PTA group. The key secondary effectiveness endpoint for ACCP at 6 months was not met (p-value = 0.0846).

Reintervention data for the two study cohorts at 12 months are tabulated below:

Table 35: Reintervention Data for the two study cohorts

	COVERA™ Group	PTA Group
Total number of access circuit reinterventions	226	242
Total number of target lesion reinterventions	93	195
Total number of reinterventions for new lesions in the access circuit	142	98
Number of subjects requiring access circuit reinterventions	100	102
Number of subjects requiring target lesion reinterventions	57	100
Number of subjects with reinterventions for new lesions in the access circuit	75	49

While the total number of reinterventions for access circuit were similar, there was a considerable reduction in the number of reinterventions for the target lesions after treatment with COVERA™ Vascular Covered Stent compared to PTA alone. However, more reinterventions for new lesions in the access circuit were required in the COVERA™ treated group compared to the PTA alone group. Secondary patency for the COVERA™ treated subjects was 94.3% and for the PTA group was 97.1%.

Your Role as a Clinician in Assuring Medical Device Safety

- Work with your professional societies & get involved in the collection of Real World Evidence via registries
- Voluntarily report adverse device related events to FDA via MedWatch
- Be attune to FDA Letters to Health Care Providers

Paclitaxel Mortality Signal in PAD

UPDATE: Treatment of Peripheral Arterial Disease with Paclitaxel-Coated Balloons and Paclitaxel-Eluting Stents Potentially Associated with Increased Mortality - Letter to Health Care Providers

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Letters to Health Care Providers

April 23, 2019 UPDATE: On June 19-20, 2019, the FDA will convene a meeting of the Circulatory System Devices Panel, to discuss and make recommendations on information related to recent observations of increased long-term mortality in peripheral arterial disease patients treated with paclitaxel-coated balloons and paclitaxel-eluting stents compared to patients treated with uncoated comparator devices. The FDA requests panel input regarding the presence and magnitude of the signal and potential causes. The FDA also seeks input regarding appropriate regulatory actions associated with the findings.

Content current as of:
03/15/2019

Questions?

robert.lee1@fda.hhs.gov

Paclitaxel Mortality Signal in PAD

- Continue diligent monitoring of patients who have been treated with paclitaxel-coated balloons and paclitaxel-eluting stents.
- When making treatment recommendations and as part of the informed consent process, consider that there may be an increased rate of long-term mortality in patients treated with paclitaxel-coated balloons and paclitaxel-eluting stents.
- Discuss the risks and benefits of all available PAD treatment options with your patients. For most patients, alternative treatment options to paclitaxel-coated balloons and paclitaxel-eluting stents should generally be used until additional analysis of the safety signal has been performed.
- For some individual patients at particularly high risk for restenosis, clinicians may determine that the benefits of using a paclitaxel-coated product may outweigh the risks.

FDA Letter to Health Care Providers March 15, 2019

Paclitaxel Mortality: AV Access Considerations

Does the potential increase in mortality from DCB use justify the benefit achieved of delaying restenosis in patients with dysfunctional AV access?

- Larger balloons need to treat veins → higher drug doses
- Potential for repeated exposure if used for recurrent venous stenosis
- Particulate embolization occurs to a different end organ
- Sicker population with more comorbidities
- Should treatment be restricted to a single exposure?

ADVISORY COMMITTEE MEETING

June 19-20, 2019: Circulatory System Devices Panel of the Medical Devices Advisory Committee Meeting Announcement

JUNE 19-20, 2019

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2017 Advisory Committee Calendar

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- Meeting Information

Date: June 19-20, 2019

Time: June 19, 2019
08:00 AM EDT – 03:00 PM EDT

Center	Date	Time	Location
CDRH	June 19, 2019 June 20, 2019	8:00 a.m. - 5:00 p.m. 8:00 a.m. - 3:00 p.m.	Gaithersburg Holiday Inn Grand Ballroom Two Montgomery Village Ave. Gaithersburg, MD 20879 301-948-8900

Content current as of:
04/22/2019

https://www.fda.gov/advisory-committees