

# **Advancing Medical Device Efficacy and Safety**

**FDA's Medical Device User Fee Act (MDUFA)  
Reauthorization Kickoff Meeting**

**October 27, 2020**

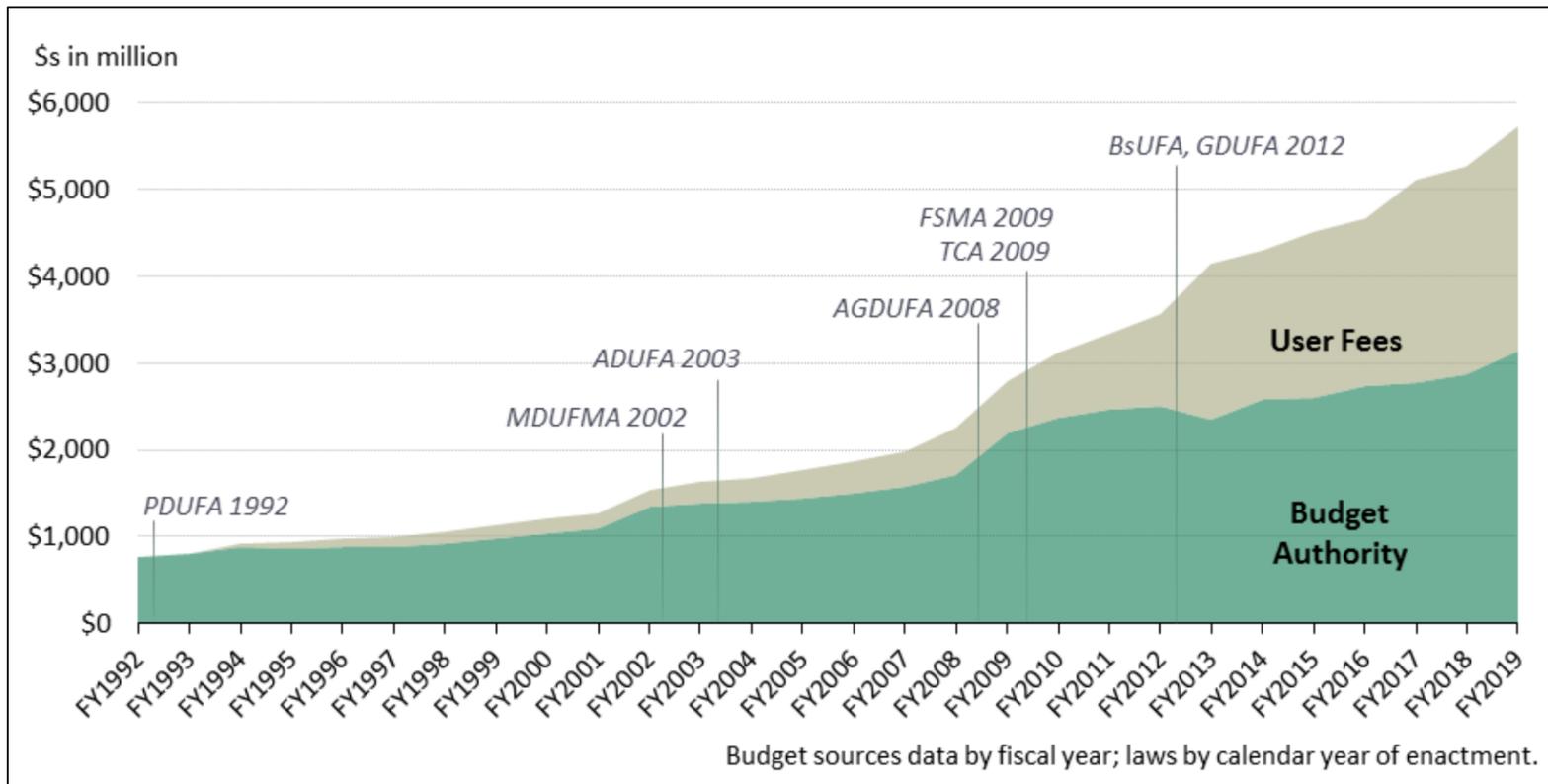
***Michael T. Abrams, MPH, PhD  
Public Citizen's Health Research Group***

***(I have no financial conflicts of interests)***

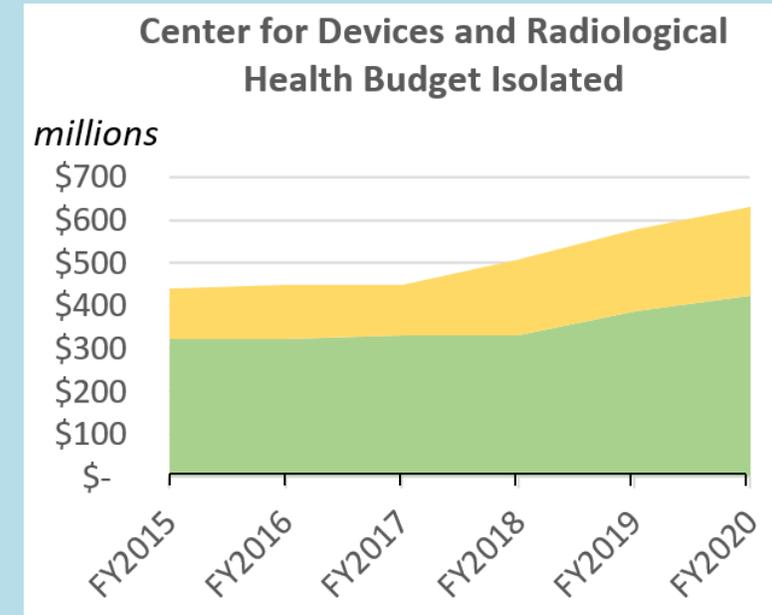


# Congressional Appropriations Versus User Fees

**Figure 1. FDA Budget, by Source, FY1992-FY2019**  
(in millions of dollars)



**Source:** Figure created by CRS using the FY1992 through FY2020 FDA CJs and the Consolidated Appropriations Act, 2019 (P.L. 116-6; H.Rept. 116-9).



**Concern:  
Industry capture**

# Background on MDUFA

- FDA regulates 190,000 different devices, 18,000 firms
- 12 new clearances or approvals per day
- MDUFA IV innovations
  - Patient engagement
  - Real world evidence {e.g., National Evaluation System for health Technology (NEST), “active surveillance”}
- Performance goal achievement...

Source: Shuren J, MDUFA IV and Beyond, FDA Video Reports, October 15, 2020, <https://www.fda.gov/industry/medical-device-user-fee-amendments-mdufa/mdufa-iv-and-beyond-video-reports>, Accessed 10/19/20.

# Not Satisfying to the Public At-Large

## Goal Performance



Submission Type	Review-Time Goal	FY 18	FY 19	FY 20	FY 21	FY 22
<b>Original PMAs, PDPs, Panel-Track PMA Supplements, and Premarket Reports</b>						
Substantive Interaction	90 calendar days	Green	Green	Yellow		
Decision with No Advisory Committee Input	180 FDA days	Green	Yellow	Yellow		
Decision with Advisory Committee Input	320 FDA days	Green	Red	Yellow		
<b>180-Day PMA Supplements</b>						
Substantive Interaction	90 calendar days	Green	Green	Yellow		
Decision	180 FDA days	Green	Yellow	Yellow		
<b>Real-Time PMA Supplements</b>						
Decision	90 FDA days	Green	Green	Yellow		
<b>De Novo Classification Requests</b>						
Decision	150 FDA days	Green	Green	Yellow		
<b>510(k) Premarket Notifications</b>						
Substantive Interaction	60 calendar days	Green	Green	Yellow		
Decision	90 FDA days	Green	Green	Yellow		
<b>CLIA Waiver by Applications</b>						
Substantive Interaction	90 calendar days	Green	Green	Yellow		
Decision with No Advisory Committee Input	150 FDA days	Green	*	Yellow		
Decision with Advisory Committee Input	320 FDA days	n/a	n/a			
<b>Dual 510(k) and CLIA Waiver by Applications</b>						
Substantive Interaction	90 calendar days	Green	Green	Yellow		
Decision with No Advisory Committee Input	180 FDA days	Green	*	Yellow		
Decision with Advisory Committee Input	320 FDA days	n/a	n/a			
<b>Pre-Submissions</b>						
Provide Written Feedback*	70 calendar days or 5 days prior to the meeting	Green	Green	Green		

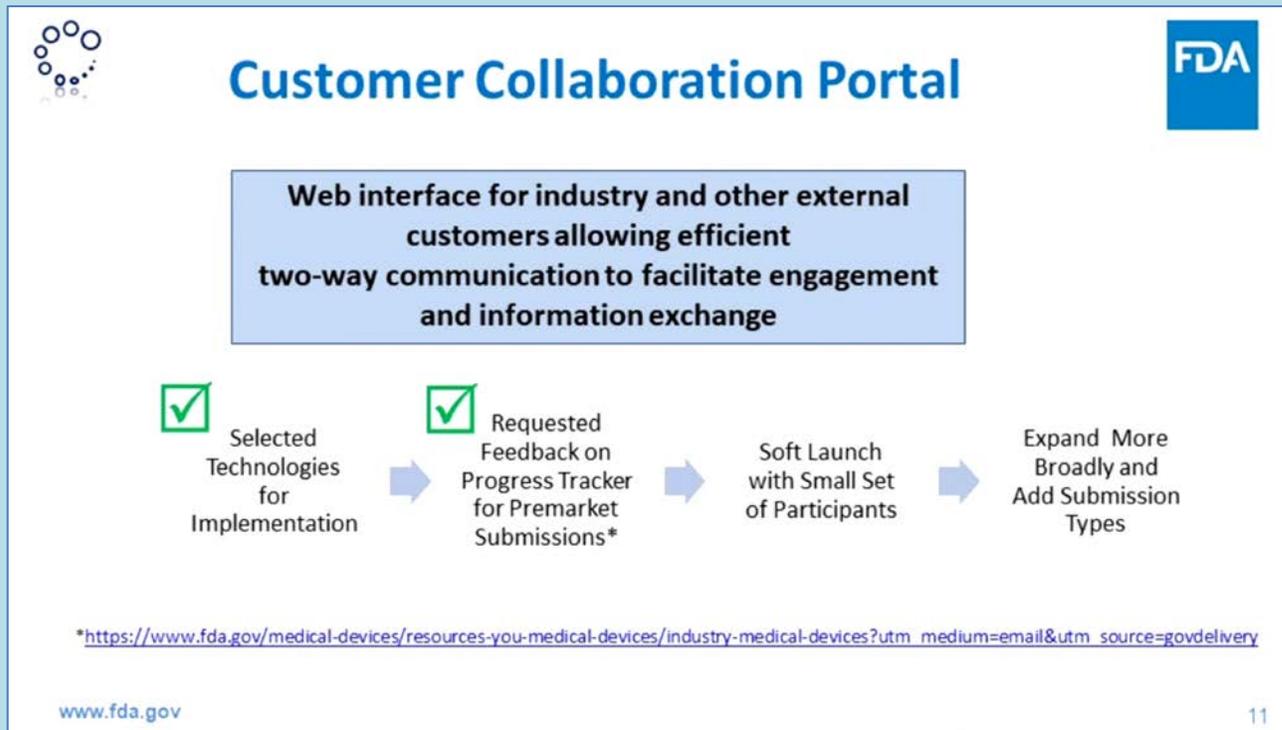
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**25 performance goals are all about time-to-action by FDA, nothing assessing public health consequences**

Source: Zimmerman B, MDUFA IV Performance Update, FDA Video Reports.

# Industry-Centered and Thus Overly Permissive

- Prime “customer” is industry, not the public as it should be
- Real world evidence (RWE) avoids more scientific rigor



**Customer Collaboration Portal**

Web interface for industry and other external customers allowing efficient two-way communication to facilitate engagement and information exchange

Selected Technologies for Implementation → Requested Feedback on Progress Tracker for Premarket Submissions\* → Soft Launch with Small Set of Participants → Expand More Broadly and Add Submission Types

[\\*https://www.fda.gov/medical-devices/resources-you-medical-devices/industry-medical-devices?utm\\_medium=email&utm\\_source=govdelivery](https://www.fda.gov/medical-devices/resources-you-medical-devices/industry-medical-devices?utm_medium=email&utm_source=govdelivery)

www.fda.gov

FDA

Source: Maisel W, Braier N, MDUFA IV: Building a Sustainable Infrastructure, FDA Video Reports.



**Ongoing Commitment to Quality**

Key Tenets of CDRH Quality

Tenet	Metric
Customer Focus	95% CDRH Customer Service Rating
Transparency	1,100+ Premarket documents managed via DCS
Standardization	200+ Staff certified by ASQ
Continuous Improvement	50+ CDRH core review, regulatory, and administrative processes improved within three years
Predictability	70%
Simplicity	

Source: Maisel W, Braier N

➤ NEST to publish assessments of RWE for premarket decision-making

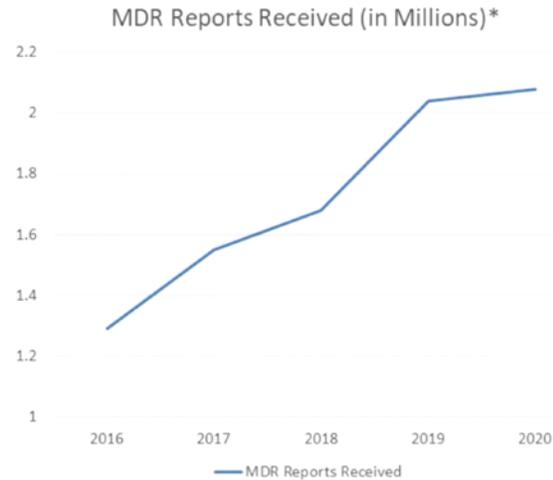
Source: Caños, D, Boyd S, Yustein R, Accessing and Using Real-World and Postmarket Data for Regulatory Decision-Making. FDA Video Reports.

# Medical Device Reports (MDRs) Taken as Signals to Respond to, Rather than Prevent Illness

## MDRs and Summary Reporting

FDA

- More than 2 million MDRs/year for device malfunctions, serious injuries and deaths that may be associated with devices
- Regulations in 21 CFR 803.19 permit FDA to grant exemptions, variances and alternatives and to include conditions
- Summary reporting
  - Aggregates events that are well understood or where other postmarket safety activities are being conducted to address the event
  - Focused use of CDRH resources on safety signals for serious or unanticipated events



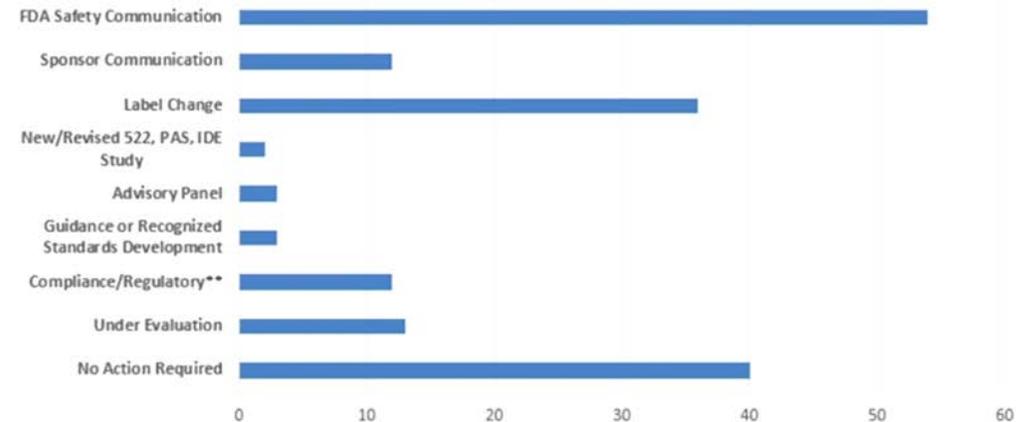
\*includes initial and supplemental reports, 2020 data projected

## Program Signals: Jan 2015- July 2020

FDA

148 Signals Entered for Evaluation

Most Common Mitigation Actions\*



\* A signal may have more than one associated mitigation action

\*\*Includes recalls, inspections, advisory action letters, sales restrictions

# Case Study: Transvaginal Mesh

- Non-absorbable surgical product for pelvic organ prolapse (POP) repair
- 2002-2011, dozens cleared for marketing under the 510(k) process absent clinical testing (Class II).
- 2011 Public Citizen petitioned FDA to ban all such products because of failed efficacy and high rates of serious complications.
- 2014 FDA denied our petition.
- 2014 FDA recategorized them to Class III. That order was finalized in 2016 and required PMAs by July 2018.
- Section 522 (of the FDCA) non-randomized studies evaluating Boston Scientific's transvaginal mesh products observed that these products did not result in better success rates than native tissue repair at one, two, and three years. (Per company's submission to FDA, February 9, 2019).
- Public Citizen testified at a February 12, 2019 FDA Advisory Committee Meeting in opposition to the use of these meshes.

# Case Study: Transvaginal Mesh (continued)

- Data presented by the FDA showed that significant adverse effects unique to the use of mesh in POP repair occurred in 3% to 15% of patients within five years of surgery.

- 77 deaths between 2008 and 2018

- Because of the FDA's recklessly inadequate actions regarding surgical mesh over nearly a decade, thousands of women have been unnecessarily harmed, many permanently. To prevent further harm the FDA should reject the pending PMAs on these devices.
- April 16, 2019 the FDA ordered that these devices could no longer be sold, 8 years after our initial complaint, and 17 years post-510(k) clearance.

	Patient Problem	Count
1	Pain	3717
2	Erosion/Exposure	3509
3	Infection	1794
4	Injury	1701
5	Incontinence	814
6	Scar Tissue	761
7	Bleeding	475
8	Infection, Urinary Tract	371
9	Disability	339
10	Neurological Deficit/Dysfunction	272

- ❖ Ten-year median lag between device approval in 93 Medical Device Safety Communications published by the FDA from 2011 to 2018. (Tau & Shepshelovich, *JAMA Int Med*, Online September 28, 2020)

# Case Study: Spinal Cord Stimulators (SCS)

- Public Citizen Report: June 10, 2020 (Carome MA)
- 1978-2019: FDA cleared 137 premarket notification submissions {510(k)} for implanted SCS with external transmitters for pain (Class II).
- 1981-2019: FDA approved six original pre-market applications (PMAs) (Class III) approved for totally implanted SCS
  - at least one based on a seriously flawed clinical study,
  - at least three based on only published scientific literature for other spinal cord stimulator systems, and the published literature was significantly flawed.
- 1980-2019: 945 of 1,008 PMA supplements were FDA approved, many of them new models.

**Major Concern: For many high-risk (Class III) stimulators FDA relied on the less rigorous ‘substantially equivalent’ standard intended for moderate-risk (Class II) devices using the 510(k) process.**

# Manufacturer and User Facility Device Experience (MAUDE) Analysis for SCS

- 2004 to 2019
- Spinal cord stimulators for pain relief

	Class II (external power supply)	Class III (implanted power supply)
Medical Device Adverse Event Reports (MDRs)	40,457	179,917
<i>Injuries</i>	38,545	118,272
<i>Deaths</i>	174	757
<i>Most common MDRs</i>	Infection, lead migration, heating, falls, lead fracture, electrical shocks, headaches	
Recalls	5	44
Class 1 recalls*	0	0
Total number of devices implanted (denominator)	?Proprietary?	

\*reasonable probability that the use of the product will cause serious adverse health consequences

# Recommendations for Medical Device Oversight

1. Request more discretionary funding for FDA.
2. Mandate more adherence to randomized control trials with definitive endpoints.
3. Require FDA to advance metrics for assessment of the benefit-to-risk ratio for clearance, approval, or rejection actions.
  - a) MDRs, RWE, and PROs useful here,
  - b) public health impact should be reported to Congress and the public, near & long-term (10 yrs).
4. Require FDA to publish their technical reviews of all PMA supplements for which the changes could alter safety or effectiveness.
5. Require industry to publicly report number of devices which are sold and implanted.
6. Reject provisions which allow lax standards for review including:
  - a) PMA approvals based on literature reviews of studies of other approved devices,
  - b) use of supplemental approval pathways for new device models,
  - c) over-reliance on post-approval MDR studies.
7. Encourage Congress to pass legislation to override *Riegel v. Medtronic*, a Supreme Court decision which limits patients' rights to sue the makers of faulty PMA devices.

# Thank you!

**Michael T. Abrams, M.P.H., Ph.D.**

Health Research Group

Public Citizen

Washington, D.C.

[mabrams@citizen.org](mailto:mabrams@citizen.org)

[www.citizen.org](http://www.citizen.org)

