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Presentation at the Medical Device User Fee Act (MDUFA) Reauthorization Kickoff Meeting

U.S. Food and Drug Administration, Via Webinar

October 27, 2020

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I am Michael Abrams a health researcher at Public Citizen. I have no financial conflicts of interest.

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Regarding MDUFA, Public Citizen has long opposed the basic tenets of this vehicle to fund FDA activities. We believe such user fees, which now fund well over half of the agency's operating budget (see left graph), too often cause the agency to place the interests of regulated industry over those of the public.

MDUFA user fees are substantial and growing (see right graph on this slide). The agency we believe should be careful to avoid expanding dependence on direct industry financing as it compromises their ability to remain objective judges of device safety and efficacy.

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Per the FDA's own characterization, the agency is responsible for ensuring the safety and efficacy of many devices. Furthermore, the agency lauds initiatives under the current MDUFA IV reauthorization including the use of more real world evidence, an idea that sounds smart and practical, but one which — especially under industry-financed influence — threatens the credibility and integrity of the medical device approval process.

And performance reviews of the MDUFA are not reassuring to the public in that regard.

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Here are examples of so-called MDUFA goal "performance" which the FDA formally reports to Congress each year. The list is dominated by benchmarks of great interest to industry — for example, how quickly decisions are issued on premarket approval applications (PMAs) — but

across the 25 total goals reported there is nothing assessing the actual public health consequences of device review decisions by the agency.

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Moreover, even now, as the FDA prepares for reauthorization, it uses language that underscores our concern that user fees have inappropriately altered the relationship between the agency and regulated industry such that medical device manufacturers are now viewed as the agency's primary "customers."

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And we know from post-clearance and approval adverse event data that harm does occur. What we do not know, however (because the performance goals do not mandate it), is how often these signals result from bad decisions of the FDA. Such performance reporting should be essential and dominant. More meaningful performance assessments are desperately needed given the serious weaknesses in the agency's premarket oversight process.

Two device case studies highlight this point.

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The first pertains to transvaginal mesh products, non-absorbable surgical implants used to repair pelvic organ prolapse in women.

Between 2002 and 2011 dozens of these implantable products were cleared for use via the 510(k) process, which does not require clinical testing.

In 2011 Public Citizen petitioned the FDA to ban all such products because of a lack of effectiveness and high rates of serious complications.

In 2014 the FDA denied our petition.

In 2016, the FDA recategorized these meshes as Class III and required submission of PMAs with data from clinical testing by July of 2018.

In 2019 the FDA convened an advisory committee meeting to review data from clinical testing of the transvaginal mesh still on the market. The industry's own data revealed these meshes did not show better success rates compared to native tissue repair.

Public Citizen testified at the February 2019 hearing in opposition to use of these meshes for the following additional reasons...

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Three to 15% of patients receiving these devices experienced significant adverse effects, the most prevalent of which are listed in the panel on the right of this slide — serious debilitating problems including ongoing or new pain and erosion/exposure of the mesh. And 77 deaths were observed related to use of the meshes between 2008 and 2018.

The middle arrow on this slide summarizes Public Citizen's review of transvaginal meshes to that 2019 advisory committee:

- 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.

In April of 2019, the FDA ordered that these meshes could no longer be sold; nearly eight years *after* our initial petition, and 17 years post-510(k) clearance. Clearly, the 510(k) process and the FDA's sluggish postmarket response to evidence of serious harm failed in this case. And, by the way, we should not be surprised that there is a substantial lag between approval of a harmful device and FDA action (see the recent *JAMA* article cited at the bottom right of this slide which found a median 10 year lag for such action).

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A second case study involves spinal cord stimulators for pain.

In June of this year Public Citizen released a detailed report examining the FDA's regulatory oversight of these devices over more than four decades.

That report observed that between 1978-2019, the FDA cleared 137 510(k) submissions for Class II implantable spinal cord stimulators for pain with an external transmitter and power source.

Between 1981 and 2019 the FDA approved six original PMAs for Class III totally implanted spinal cord stimulators for pain, even those approvals were based on very weak clinical evidence. One of the earliest PMAs was based on a seriously flawed clinical study. Three later original PMA approvals were based on only published scientific literature for <u>other</u> spinal cord stimulator systems, and that literature was also significantly flawed.

From this analysis comes the major concern that:

> For many high-risk stimulators the FDA essentially relied on the less rigorous 'substantially equivalent' standard intended instead for moderate-risk devices.

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The report also examined MAUDE (Manufacturer and User Facility Device Experience) data from 2004 to 2019 to discern concerning adverse event signals related to spinal cord stimulators for pain, revealing hundreds of thousands of injuries and several hundred deaths. Surprisingly though, there were no Class 1 recalls issued by the FDA, a finding which seems incredible to us given the widespread use of these demonstrably risky surgical implants.

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In summary, we make the following recommendations regarding the FDA's device approval process:

1. Seek more discretionary funding, rather than user fees, to cover essential activities.

2. Mandate more randomized control trials with definitive endpoints for all high-risk, permanently implanted devices.
3. Require the FDA to advance performance measures that assess benefit-to-risk ratios for the devices they clear, approve, or reject. Emphasize public health impact of such decisions for at least 10 years after those decisions are rendered.
4. Require FDA to publish technical reviews of PMA supplements for which changes could alter safety and effectiveness (per our work on spinal cord stimulators)
5. Require industry to publicly report the number of devices sold and implanted (to facilitate evaluations).
6. Reject provisions which allow lax standards of review including: (a) PMA approvals based on literature reviews, (b) PMA supplements for new device models, and (c) over-reliance on post-marketing surveillance over more rigorous premarket clinical trials.
7. And finally, any federal device legislation proposed should include an override of the *Riegel v. Medtronic* Supreme Court decision which limits a patients' rights to sue a maker of a faulty PMA device.

Too often, high-risk permanently implanted devices have insufficient premarket clinical evidence to provide a reasonable assurance of safety and effectiveness. The device clearance and approval processes at the FDA must evolve to address these insufficiencies.

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My contact information. Thank you.