

April 25, 2022

The Honorable Patty Murray  
Chair  
Committee on Health, Education, Labor  
and Pensions  
United States Senate  
Washington, D.C. 20510

The Honorable Richard Burr  
Ranking Member  
Committee on Health, Education, Labor  
and Pensions  
United States Senate  
Washington, D.C. 20510

**RE: Comments Regarding Reauthorization of the Prescription Drug User Fee Act and  
Medical Device User Fee Amendments**

Dear Chairperson Murray and Ranking Member Burr:

Public Citizen, a consumer advocacy organization with more than 500,000 members and supporters nationwide, respectfully submits the following comments regarding pending legislation that would reauthorize the Prescription Drug User Fee Act and the Medical Device User Fee Amendments for fiscal years 2023 to 2027 (PDUFA VII and MDUFA V, respectively).

Since July 2020, Public Citizen has participated in the Food and Drug Administration's (FDA's) public stakeholder consultation meetings with patient and consumer advocacy groups regarding PFUFA VII and MDUFA V. Based on our involvement in these meetings and our deep knowledge of the FDA's prescription-drug and medical-device regulatory processes, we have serious concerns regarding the protracted, nonpublic negotiations that occurred between the FDA and the pharmaceutical-device and medical-device industries prior to the release of the agency's PDUFA VII and MDUFA V commitment letters.

As a result of the regulatory capture that has been fostered by the FDA's heavy reliance on user fees, the PDUFA VII and MDUFA V reauthorization proceedings once again have been skewed heavily towards placating the interests of the prescription-drug and medical-device industries with ever faster, and too often hasty, reviews of marketing applications. In contrast, the agency has ignored recommendations from Public Citizen and other consumer advocacy groups for improving the premarket and postmarket regulatory oversight of prescription drugs and medical devices to better ensure that these products are safe and effective.

This month, Mitchell and colleagues published an in-depth analysis of the original passage of PFUFA and all subsequent PDUFA reauthorization legislation and related activities.<sup>1</sup> Based on their review, these authors concluded that:

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<sup>1</sup> Mitchell AP, Trivedi NU, Bach PB. The Prescription Drug User Fee Act: much more than user fees. *Med Care*. 2022 Apr 1;60(4):287-293.

The majority of policy changes enacted through PDUFA legislation have favored industry through decreasing regulatory standards, shortening approval times, and increasing industry involvement in FDA decision-making...

The analysis of PDUFA's history raises enough serious questions about PDUFA's overall impact on US drug regulatory policy that policymakers should reconsider perpetuating this system... and reallocate the necessary funds to relieve FDA of its financial reliance on industry.

Having been directly involved in the reauthorization process for both PDUFA VII and MDUFA V, we concur with Mitchell and colleague's critical assessment of these user fee programs. To mitigate regulatory capture at the FDA, we encourage your Committee to provide considerably greater direct taxpayer-funded appropriations to the FDA to decrease the agency's financial dependence on regulated industries. We further urge your Committee to craft PDUFA VII and MDUFA V reauthorization language that would do the following:

- (1) To ensure the integrity and objectivity of critical review decisions, require the FDA to designate separate groups of staff for (a) providing advice, guidance and technical assistance to sponsors prior to the submission of new drug applications (NDAs), biologics licensing applications (BLAs), premarket approval applications (PMAs), or 510(k) premarket notification submissions and (b) reviewing and making decisions on any subsequent related NDA, BLA, PMA, or 510(k) premarket notification submission. An operational firewall then should be created between the FDA staff involved in any presubmission interactions and those involved in the postsubmission NDA, BLA, PMA, or 510(k) premarket submission review and decision-making.
- (2) Require FDA staff training on how to minimize the risk of regulatory capture of the agency by sponsors.
- (3) Require periodic routine surveys of FDA staff and advisory committee members to obtain their candid perspectives on the adequacy of the Agency's review and decision-making processes.

We offer the following additional specific comments for your consideration as you craft legislation for PDUFA VII and MDUFA V.

## **PDUFA VII**

As your Committee deliberates on the PDUFA VII legislation, we recommend that you consider including provisions in the legislation that would do the following:

- (1) Add additional performance measures to assess the actual short- and long-term public health impacts of the FDA's decisions regarding drugs and biologics, such as the following:
  - (a) Counts and percentages of NDAs/BLAs reviewed each year that were rejected because there was a lack of evidence establishing safety or efficacy.
  - (b) Counts and percentages of NDAs/BLAs reviewed each year that were the subject of subsequent FDA warnings or withdrawals during the first several years post-approval.

- (c) Counts and percentages of NDAs/BLAs reviewed each year approved with at least two phase 3 randomized, controlled clinical trials demonstrating consistent and robust evidence of safety and efficacy and favorable benefit-risk profiles, and those with one or fewer such clinical trials
  - (d) Counts and percentages of those NDAs/BLAs reviewed each year subject to mandated post-marketing studies where those obligations were fulfilled in the prespecified time allotted and that confirmed safety and efficacy.
  - (e) Counts and percentages of NDAs/BLAs reviewed each year for which the FDA decision regarding approval was concordant with advisory committee recommendations
- (2) Revise the PDUFA reauthorization negotiation process to make all meetings between industry and the FDA fully open to the public. At present the regulated industry and the FDA hold closed meetings in which they hammer out specifics regarding the program's budgeting, personnel, and overall operation goals. This asymmetry of influence for industry versus patients and the broader American public is completely inappropriate and unacceptable.
  - (3) Direct the FDA to commission objective studies that quantify the avoided or realized harms resulting from new NDA/BLA approval decisions. Third-party researchers should be regularly commissioned to conduct independent reviews of public health performance indicators tied directly to the FDA's decisions.
  - (4) Require the FDA to repropose and promptly finalize a rule allowing generic-drug manufacturers to update product labeling promptly to reflect certain types of newly acquired information related to drug safety, irrespective of whether the revised labeling differs from that of the reference-listed drug, in advance of the FDA's review of the changes through a "changes being effected" (CBE-0) supplement. The FDA currently does not allow generic drug manufacturers to initiate safety updates to product labeling when they become aware of new risks, although brand-name manufacturers have long had that ability and responsibility. Although the FDA in 2013 proposed a new rule to correct this safety gap,<sup>2</sup> the rule was not finalized and was later withdrawn in 2018.
  - (5) Provide the FDA with mandatory recall authority for all prescription and over-the-counter drugs (for example, see the Protecting Americans from Unsafe Drugs Act, which was introduced in February by Rep. Andy Kim and passed by the House as part of H.R. 4521, the America COMPETES Act of 2022).
  - (6) Strengthen the FDA's accelerated-approval pathway by:
    - (a) Only allowing accelerated approval of a drug based on a surrogate endpoint when there is widespread, evidence-based agreement in the research community that an effect on a particular surrogate endpoint is reasonably likely to predict clinical benefit.
    - (b) Requiring sponsors to conduct well-controlled post-approval studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit.
    - (c) Providing the FDA with explicit authority to require such post-approval studies begin prior to accelerated approval.

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<sup>2</sup> 78 FR 67985.

- (d) Providing the FDA with explicit authority to withdraw approval on an expedited basis if the sponsor fails to achieve agreed-upon enrollment targets, milestones, or timely study completion.
- (e) Mandating automatic expiration of approval one year after any target date of post-approval study completion and not later than five years after approval unless certain conditions are met.
- (7) Minimize reliance on Risk Evaluation and Mitigation Strategies mandated in lieu of premarket resolution of safety concerns. Industry too often is allowed to delay safety studies while it reaps tremendous profits on prematurely approved drugs and biologics.
- (8) Add performance indicators that specifically report each year on the number of novel BLAs/NDAs that specifically address illnesses that impact minority and other neglected populations (e.g., sickle cell disease therapies or treatments for ovarian cancer) and that report how often pivotal clinical trials enroll representative proportions of minorities. These performance measures will help the FDA ensure that results of clinical trials supporting approval of new drugs are generalizable to minority populations.
- (9) Implement the National Academies of Science, Engineering, and Medicine's public health framework for regulatory oversight of opioids. This framework will enhance the Agency's stated goal to ensure that the review of drugs and biologics appropriately considers the benefits and risks associated with such products before they are approved for marketing.
- (10) Provide the FDA with the budgetary resources to strengthen and reaffirm the agency's commitment to timely, rigorous, in-person inspections of manufacturing facilities to ensure the safety and quality of prescription drugs.

## **MDUFA V**

On June 10, 2020, we forwarded to your Committee our detailed report documenting the FDA's dangerously lax regulatory oversight of high-risk implanted spinal cord stimulators for pain relief that had resulted in unacceptable risk to patients.<sup>3</sup> Our report illustrated that the FDA's regulatory oversight of implanted spinal cord stimulators for pain relief had had serious, wide-ranging deficiencies since the enactment of the Medical Device Amendments of 1976 and was emblematic of what's wrong with the agency's oversight of medical devices and the serious harm to patients that can result. Our 2020 report concluded with a series of recommendations to better ensure the safety and effectiveness of high-risk, permanently implanted devices.

As your Committee deliberates on the MDUFA V legislation, we recommend that you consider including provisions in the legislation that would do the following:

- (1) Require submission of premarket approval applications (PMAs) for all high-risk, permanently implanted medical devices and the inclusion of data from well-designed, randomized controlled trials in such PMA submissions.
- (2) Require the FDA to make publicly available (a) summary review memoranda for all PMA supplements for all Class III medical devices, and (b) summary and safety and

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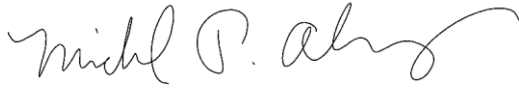
<sup>3</sup> [https://www.citizen.org/wp-content/uploads/2526\\_200610\\_Spinal-Cord-Stimulator-Report\\_FINAL.pdf](https://www.citizen.org/wp-content/uploads/2526_200610_Spinal-Cord-Stimulator-Report_FINAL.pdf).

effectiveness data for any approved PMA supplements for which the device is modified in ways that could alter its safety or effectiveness.

- (3) Require the FDA to perform and publish comprehensive analyses and assessments of adverse events from all approved PMAs and PMA supplements, PMA annual reports, and the agency's Manufacturer and User Facility Device Experience (MAUDE) database.
- (4) Require the FDA to revamp its online MAUDE database to make it more user friendly.
- (5) Require the FDA to compile and make publicly available a list of all Class III devices for which PMA approval was granted based on literature reviews of studies assessing devices other than the one for which PMA approval was sought, rather than well-designed prospective clinical trials of the actual devices for which PMA approval was sought.
- (6) To provide an essential context for understanding numbers of medical-device adverse-event reports submitted to the FDA for each type of medical device, require the FDA to take the following steps:
  - (a) Make available to the public the PMA annual report information (required for approvals since August 1, 2009) that reveals the number of devices shipped or sold, as well as the number of devices actually implanted, if available.
  - (b) Implement a regulation requiring that each permanent implantation of a medical device be reported by device-user facilities to a publicly accessible database maintained by the FDA.
- (7) Nullify the Supreme Court's 2008 decision in *Riegel v. Medtronic*, which held that the existing law preempts the right of patients to bring damages claims against medical-device manufacturers for injuries caused by high-risk medical devices marketed pursuant to a PMA. The Riegel decision ended a period of more than 30 years in which federal and state laws had worked hand in hand to strengthen device safety. The multiple dangerous weaknesses in the FDA's regulatory oversight of medical devices make the preemption decision in Riegel a dangerous outcome for patients.
- (8) Require the creation of a database of predicate devices for 510(k) premarket submission that is to be used by the FDA to issue annual performance reports revealing the quality and appropriateness of legacy predicate devices as a foundation for 510(k) premarket clearance decisions.
- (9) Establish MDUFA performance measures that capture public health indicators related to the benefits and harms of medical devices that have been cleared, approved, recalled, and rejected.
- (10) Establish MDUFA performance measures that offer year-over-year indicators regarding advisory committee members' and agency reviewers' perceptions regarding medical-device regulatory decisions made by the FDA.
- (11) Establish MDUFA performance measures that assess long-term (three or more years) public health impacts of medical devices that have been approved or cleared for marketing.
- (12) Provide the FDA with the budgetary resources to strengthen postmarket activities, including timely monitoring of postmarket clinical trials, adverse-event monitoring, and the device recall system (including consumer notification).
- (13) Provide the FDA with the budgetary resources to strengthen and reaffirm the agency's commitment to timely, rigorous, in-person inspections of manufacturing facilities to ensure the safety and quality of medical devices.

We encourage your Committee to take our recommendations into consideration when crafting legislation for PDFUFA VII and MDUFA V.

Sincerely,

A handwritten signature in black ink, appearing to read "Michael T. Abrams".

Michael T. Abrams, M.P.H., Ph.D.  
Senior Health Researcher  
Public Citizen's Health Research Group

A handwritten signature in black ink, appearing to read "Michael A. Carome".

Michael A. Carome, M.D.  
Director  
Public Citizen's Health Research Group

cc: Members, Senate HELP Committee