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Public Meeting on Prescription Drug User Fee Act (PDUFA) Reauthorization

U.S. Food and Drug Administration, Via Webinar

July 23, 2020

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Thank you. I am Michael Abrams, a researcher with the Health Research Group at Public Citizen, a nonprofit consumer advocacy organization with more than 500,000 members and supporters nationwide. Since 1971 we have advocated on a range of federal issues including those concerning the Food and Drug Administration (FDA). We do not receive contributions from industry and have no conflicts of interest.

Regarding the Prescription Drug Use Fee Act (PDUFA), Public Citizen has long opposed the basic tenets of this vehicle to fund FDA activities. We believe such user fees, which now directly fund well over half of the agency's operating budget, too often cause the agency to place the interests of regulated industry over those of the public. Stated another way, Public Citizen continues to strongly oppose any government agency being funded directly by the industry it regulates.

Our advice for PDUFA VII is that it includes provisions that better promote the mission of the FDA and the public health interests of the U.S. population. Certainly, the stakes are substantial.

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In FY2019 the FDA's obligated user fee revenues for activities related to human drugs exceeded $1 billion, and these revenues funded over 4,000 full-time professionals at the FDA. The chart here shows the number of new drug or biologic applications tendered-- 166 represented in the last bar for FY 2019, with priority applications on the increase. Note further that per the FDA's actual budget in FY2019, 64% of all money focused on human drug issues come directly from PDUFA and other user fees.[1]

[1] https://www.fda.gov/media/135078/download, table on page 27

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The FDA submits annual reports to Congress. Here are three exhibits from their FY2019 performance document. The left table lists hundreds of meetings and shows that FDA professionals are timely in scheduling gatherings and completing follow-up activities. The right two charts present PDUFA performance data that typically garner the most attention. Both charts show annualized data from 10 recent years ending in FY2018. The top right chart presents time to application review with yearly medians of about 7 months for priority drugs and 11 months for standard drugs. The chart below shows that most of the priority-review drugs, and over half of the standard-review drugs, are approved in the first cycle of review. These numbers suggest efficient approval pipelines, but from a consumer perspective such data presentations seem to avoid the opportunity to assess how PDUFA actions have impacted human health. We believe instead consumers wants to know whether truly beneficial drugs emerged, and whether bad or questionable drugs were approved. How many and how fast is important, but quantitation of health gains (and harms) is essential. One immediate approach to collecting data about the quality of a review cycle in the near-term is to survey the experts who directly contribute to the scientific decision-making process.

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Such surveys should afford FDA reviewers the opportunity to provide anonymous comments on the agency's review process each cycle. Past anonymous surveys conducted by Public Citizen and the HHS's Office of the Inspector General revealed that a substantial proportion of expert FDA reviewers were concerned about the drug review process under PDUFA. Results from those two surveys are summarized on this slide. The surveys showed that in 1998 64% of FDA medical officers felt increasing pressure to approve new drugs, and in the early 2000s 36% of CDER reviewers were <u>not</u> confident in FDA decisions regarding drug safety.

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And these concerns persist in this era of PDUFA VI in both lay and academic publications. This slide offers notable points made by a 2018 *Propublica* report and a 2020 *Journal of the American Medication Association* study. Propublica's investigative journalist wrote this statement: "The FDA is increasingly green-lighting expensive drugs despite dangerous side effects and inconclusive evidence…," even as Dr. Janet Woodcock, the long-time director of CDER said that "Clearly, accelerated approval has greater uncertainty." Policy and medical researchers have observed, amazingly, that at the FDA there is a "built-in fear of regulation". …and one former FDA medical team leader actually said this: "You don't survive as a senior official at the FDA unless you are pro-industry." These points demonstrate that pharmaceutical largess is at least somewhat ensconced at the FDA in a way that negatively impacts the agency's mission.

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Studies and surveillance of the FDA's review and approval process have revealed negative impacts of PDUFA. In 2014, a *Health Affairs* report by Frank and colleagues studied over 700 new drug approvals between 1975 and 2009 and divided them into pre- and post-PDUFA

epochs. They then searched for negative events attached to each approved drug in two forms, either the addition of a boxed warning or the drug's withdrawal from the marketplace. What they found is summarized by this graph. During the first 4 years both pre- and post-PDUFA drugs experienced about a 5% probability of a warning or withdrawal, but beyond that point post-PDUFA approvals always performed more poorly than drugs approved before the law was implemented.

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Additionally, we know from simple FDA Adverse Event Reporting System (FAERS) data, pictured here, that since the 1990s serious events and even deaths have increasingly been linked to pharmaceutical use. I show this graph not to infer causality, but instead to remind us that these simple trends reveal little about what lies beneath. Consumers and the FDA need to know if and how these adverse event trends relate to changes in the drug review process. Such analyses should be regularly used to assess the performance of the PDUFA program.

Identifying those correlations, of course requires advanced data processing methods that are on FDA's radar via programs like the Sentinel and real-world data analytics initiatives. Public Citizen supports those initiatives, but only as tools to complement the FDA's principal and statutory role as a gatekeeper for new drug products. This gate-keeping function, by contrast, must be reliant on rigorous randomized trials.

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Accordingly, Public Citizen strongly advocates the following for PDUFA VII:

- More taxpayer-supported spending for the agency to decrease user fee dominance and dependence.
- More adherence to pre-market requirements for at least two large, randomized, blinded trials with definitive clinical endpoints.
- Requirements that the FDA have independent organizations conduct anonymous surveys of their reviewers.
- Establish FDA authority to order drug recalls.
- Direct the FDA to create regulations that allow generic drug manufacturers to update product labeling with safety information.
- Establish an opioid-specific regulatory framework
- Require the FDA to assess the benefit-to-risk ratios linked to drug approval actions.
- And finally today, we caution against any provisions that might:
    - Loosen restrictions on off-label promotion
    - Create time-limited provisional approval pathways (as proposed in H.R. 7296).
    - Create pathways that extend manufacturer monopoly pricing powers.

In summary, Public Citizen believes that future PDUFA-related legislation must enable the FDA to re-assert its ethos as a strong gate-keeper for new drugs that are safe, effective, and truly advance human health.

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Thank you. Here is my contact information.