



1600 20th Street, NW • Washington, D.C. 20009 • 202/588-1000 • [www.citizen.org](http://www.citizen.org)

**Public Meeting on the Recommendations for Prescription Drug User Fee Act (PDUFA)  
Reauthorization: Draft Commitment Letter Review**

**U.S. Food and Drug Administration, Via Webinar**

**September 28, 2021**

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

**Title slide**

Good afternoon, I'm Michael Abrams, Senior Health Researcher at Public Citizen's Health Research Group. I have no financial conflicts of interest.

**Slide 2**

We have many suggestions to improve the draft PDUFA commitment letter beginning with the performance measures used to set goals. The currently proposed measures are simplistic timeline quotas focused on pleasing the regulated industry's desire for fast reviews, such as:

the percentage of standard new drug applications (NDAs)/biologic licensing applications (BLAs) acted upon within 10 months of submission.

Additional performance measures should be developed to assess the actual short- and long-term public health impact of the Food and Drug Administration's (FDA's) decisions regarding drugs and biologics.

We offer the following five examples of such public health performance measures:

1. % of NDAs/BLAs which were rejected because there was a lack of evidence establishing safety or efficacy
2. % of previously approved NDAs/BLAs that were the subject of subsequent FDA warnings or withdrawals during the first several years post approval
3. % of NDAs/BLAs approved with at least two phase 3 randomized, controlled trials demonstrating consistent and robust evidence of safety and efficacy and favorable benefit-risk profiles
4. % of NDAs/BLAs subject to mandated post-marketing studies where those obligations were fulfilled and confirmed safety and efficacy
5. % of NDAs/BLAs for which the FDA decision regarding approval was concordant with advisory committee recommendations

### Slide 3

Related to FDA reviewer and advisory committee activities, we recommend that the Agency develop performance measures based on surveys of FDA reviewers and advisory committee members about their experiences reviewing NDAs/BLAs. Past surveys have been too infrequent and concerning. In 2003, for example, a Department of Health and Human Services Office of Inspector General Report found that among 136 Center for Drug Evaluation and Research reviewers surveyed, only 64% were confident in FDA decisions regarding the safety of a drug.<sup>1</sup> In 2018, a former FDA medical team leader told *ProPublica*, “you don’t survive as a senior official at the FDA unless you’re pro-industry.”<sup>2</sup> Candid FDA staff and advisory committee member perspectives on the adequacy of the Agency’s review and decision-making processes are certainly germane to Program performance and thus should be measured and presented to the public on a regular basis. Important measures that could be derived from routine surveys include the following:

1. % of reviewers who had concerns about FDA NDA/BLA decisions related to safety or efficacy
2. % of reviewers who felt they were free from direct or indirect pressure from the regulated industry when reviewing NDAs/BLAs
3. % of reviewers or committee members who felt they had ample time and resources to review the NDAs/BLAs they were assigned
4. % of reviewers or committee members who felt their concerns about NDAs/BLAs were properly ascertained and respected by FDA decision-makers

### Slide 4

More generally, the commitment letter language should be recast to emphasize the FDA’s regulatory role and responsibility. Presently, for example, it has prominent language like this:

“The goal of the Program is to promote the efficiency and effectiveness of the first cycle review process and minimize the number of review cycles necessary for approval, ensuring that patients have timely access to safe, effective, and high-quality new drugs and biologics.”<sup>3</sup>

---

<sup>1</sup> Office of Inspector General. *FDA’s Review Process For New Drug Applications*. Department of Health and Human Services. March 2003. Publication OEI-01-01-00590.

<sup>2</sup> Chen C. FDA repays industry by rushing risky drugs to market. *ProPublica*. June 26, 2018. <https://www.propublica.org/article/fda-repays-industry-by-rushing-risky-drugs-to-market>. Accessed September 24, 2021.

<sup>3</sup> Food and Drug Administration. PDUFA reauthorization performance goals and procedures fiscal years 2023 through 2027. <https://www.fda.gov/media/151712/download>. Accessed September 24, 2021.

Such language should be modified by adding that a primary Program goal is to protect public health by minimizing the probability that unsafe or ineffective drugs or biologics enter the market.

Moreover, the commitment letter should state that although the Agency offers technical assistance to NDA/BLA sponsors in the preparation of their applications, ensuring the quality of the NDA/BLA is ultimately the responsibility of the sponsor, not of the FDA.

### **Slide 5**

There are several places in the commitment letter where “expediting drug development” is the clear goal including under Section K. “Enhancing regulatory science...” Such language suggests the Agency is responsible for “...ensuring the sustained success of the breakthrough therapy program, ... use of new surrogate endpoints as the primary basis for product approval, ...and exploring the use of real-world evidence for use in regulatory decision-making.”<sup>4</sup>

Such goals should be revised by adding statements limiting surrogate endpoint use to those that have been scientifically validated and deemed by the majority of the medical community to be predictive of clinically meaningful outcomes. It should further caution that real-world evidence must not supplant well-designed randomized controlled trials (RCTs) to establish safety and efficacy of each product’s FDA-approved indications, and affirm at least two phase 3 RCTs as the usual standard for demonstrating substantial evidence of effectiveness.

The need for these cautions and standards is supported by research which shows that 81% of NDA approvals in 2018 involved Accelerated Approval, Fast-Track, or Priority Review,<sup>5</sup> and that faster approvals under PDUFA correlated with the marketing of products that were less safe than those marketed before the PDUFA was instituted.<sup>6</sup>

### **Slide 6**

The draft commitment letter states: “FDA’s philosophy is that timely interactive communication with sponsors during drug development is a core Agency activity to help achieve the Agency’s mission to facilitate the conduct of efficient and effective drug development programs.”<sup>7</sup>

The FDA’s review and approval of the BLA for aducanumab for treatment of Alzheimer’s disease revealed that such interactive communications established under PDUFA have resulted in inappropriately close collaborations between the Agency and sponsors that have compromised the integrity for NDA/BLA reviews.

To address this problem, the commitment letter should be modified to include provisions that:

---

<sup>4</sup> *Ibid.*

<sup>5</sup> Darrow JJ, Avorn J, Kesselheim AS. FDA approval and regulation of pharmaceuticals, 1983-2018. *JAMA*. 2020;323(2):164-176.

<sup>6</sup> Frank C, Himmelstein DU, Woolhandler S, et al. Era of faster FDA drug approval has also seen increased black-box warnings and market withdrawals. *Health Aff (Millwood)*. 2014;33(8):1453-1459.

<sup>7</sup> Food and Drug Administration. PDUFA reauthorization performance goals and procedures fiscal years 2023 through 2027. <https://www.fda.gov/media/151712/download>. Accessed September 24, 2021.

1. Characterize the FDA's primary role as being the gate-keeper, watchdog, and judge of industry products (to assert and codify its objectivity and independence)
2. Establish procedures that separate (with a firewall between) staff involved in pre-NDA/BLA-submission interactions with sponsors from staff who formally review those applications for regulatory decision-making purposes
3. Require FDA staff training on how to minimize the risk of regulatory capture of the Agency by sponsors

**Slide 7**

Finally, here are several more actions the FDA should pursue as part of the PDUFA reauthorization process:

1. Seek more discretionary program funding from Congress to decrease its financial dependence on regulated industry
2. Revise the reauthorization negotiation process to make the meetings between industry and the FDA fully open to the public
3. Implement the National Academies of Science, Engineering, and Medicine's public health framework for regulatory oversight of opioids
4. Maintain in-person manufacturing facility inspection requirements
5. Commission objective studies that quantify the avoided or realized harms resulting from NDA/BLA approval decisions
6. Minimize reliance on REMS mandates in lieu of premarket resolution of safety concerns

**Slide 8**

My contact information. Thank you.