

Congress of the United States
House of Representatives
Washington, DC 20515-0902

Robert M. Califf, MD
Commissioner U.S. Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993

September 29th, 2023

Dear Commissioner Califf,

I write in support of the recommendations outlined in the U.S. Food and Drug Administration (FDA) Citizen Petition filed by Columbia Law School's Science, Health, and Information Clinic on behalf of Universities Allied for Essential Medicines (UAEM) on February 27, 2023, referenced under docket number FDA-2023-P-0660. The recommendations outlined in this petition will enhance the authority awarded by Congress to the FDA in ensuring clinical trial sponsor compliance to requirements for timely clinical trial results reporting under the FDA Amendments Act (FDAAA) of 2007.

This year alone, Congress has allocated nearly \$54 billion for biomedical research, including more than \$47.5 billion to the National Institutes of Health (NIH),¹ of which some 85% are granted to universities and laboratories operating outside of the agency's institutes themselves.² Results of any clinical trials funded by these grants are required to be reported under FDAAA. To understand the impact of this investment, it is critical that the results of these federally funded clinical trials be reported in an accurate and timely fashion to the ClinicalTrials.gov database.

Additionally, patients and clinicians rely on the ClinicalTrials.gov database to make informed decisions about health and safety. However, those decisions rely upon up-to-date and complete information. To date, more than 4,000 clinical trials on this public database are missing results due to deficiencies in reporting and an ineffective FDA response to date.³ As an additional tool to compel trial sponsors to report results, the FDA

¹ NIH, Impact of NIH Research, <https://www.nih.gov/about-nih/what-we-do/impact-nih-research> (last accessed June 14, 2023)

² NIH, Budget, <https://www.nih.gov/about-nih/what-we-do/impact-nih-research> (last accessed May 15 2023)

³ <https://fdaaa.trialstracker.net/>

could have levied \$46 billion in fines.⁴ Only 92 Pre-Notices and 4 Notices of Noncompliance have been issued to current trial sponsors.⁵

Nevertheless, these Pre-Notices of Noncompliance have been remarkably effective in compelling sponsors to report results. A recent study, which obtained the few dozen Pre-Notices issued by the FDA between 2013 and 2021, found that these warning letters led to recipients submitting results with over a 90 percent reporting rate.⁶ Additionally, the 4 Notices of Noncompliance led to the few recipients who had failed to submit results after receiving an initial Pre-Notice to quickly comply with results reporting requirements under FDAAA.

The NIH and FDA's limited enforcement of FDAAA has been examined in an Office of Inspector General August 2022 report, a January 2023 letter from Representative and Ranking Member of the House Energy and Commerce Committee Frank Pallone, and an April 2023 report from the Government Accountability Office.^{7 8} At each instance, the NIH and FDA have been encouraged to further develop enforcement actions. In response, the NIH has begun to take meaningful steps toward improving compliance of results reporting from clinical trials funded by the agency.⁹ The FDA must also similarly take action to address the backlog of thousands of clinical trials with missing and overdue results. The NIH has created a robust plan to improve compliance by establishing a centralized review process of registration and results reporting. As a means of streamlining results reporting, the NIH has created a quarterly review of all agency grant-funded trials that have not submitted results to ClinicalTrials.gov within their submission deadline along with the sending notices of potential noncompliance. The FDA should follow suit, by implementing the recommendations outlined in the petition to demonstrate a commitment to clinical trial transparency.¹⁰

Given the public safety and budgetary consequences of noncompliance, the FDA must move promptly to grant this petition and enact the following:

1. Order and organize offices to increase enforcement of clinical trials results reporting by issuing more Pre-Notices and Notices of Noncompliance and imposing civil money penalties when appropriate. More specifically, FDA should begin sending out a minimum of 250 such Pre-Notices annually, at least until compliance

⁴ <https://fdaaa.trialstracker.net/>

⁵ <https://www.statnews.com/pharmalot/2023/01/24/children-pediatrics-transparency-clinical-trials-fda-nih/>

⁶ <https://jamanetwork.com/journals/jama/fullarticle/2786399>

⁷ <https://oig.hhs.gov/oas/reports/region6/62107000.asp>

⁸ <https://www.gao.gov/products/gao-23-105656>

⁹ <https://www.statnews.com/pharmalot/2022/11/07/nih-clinical-trials-transparency-fda-2/>

¹⁰ <https://nexus.od.nih.gov/all/2023/03/24/nih-clinical-trials-reporting-compliance-a-shared-commitment/>


- materially improves. For those sponsors who fail to respond to Pre-Notices, FDA should promptly issue Notices of Noncompliance and impose civil money penalties on those who refuse to comply even after receiving a Notice of Noncompliance.
2. Order the drafting and issuance of a new guidance document which explains how FDA will direct its enforcement efforts, clearly outline a prioritization framework such that federally-funded clinical trials and those with significant consequences for patients are prioritized.
 3. Create a public dashboard of all Pre-Notices sent by the FDA that is routinely updated to also reflect whether the sponsor addressed the issue of potential noncompliance.

Just before the agency's self-imposed deadline of 180 days from filing, on August 26th, 2023, as per 21 C.F.R. 10.30 ("Citizen petition"), the FDA issued an interim notice to UAEM.

While FDA failed to issue a formal written response, we have reviewed the interim notice which stated the agency would "require additional time" to respond to the citizen petition.

In light of this delay, we urge FDA to address long-standing results reporting deficiencies by exacting the recommendations in the petition and issue a timely formal response.

Sincerely,

A handwritten signature in blue ink, appearing to read "Neal P. Dunn". The signature is stylized and cursive.

Neal P. Dunn, M.D.
Member of Congress