

TRANSFORMING CLINICAL TRIAL RESULTS REPORTING IN THE UNITED STATES

EXAMINING THE U.S. FOOD AND DRUG ADMINISTRATION AND NATIONAL INSTITUTES OF HEALTH'S ENFORCEMENT OF CLINICAL TRIAL REPORTING LAWS



Science, Health & Information Clinic



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Universities Allied for Essential Medicines (UAEM) is honored to collaborate with Columbia Law School's Science, Health, and Information Clinic (SHIC) and the Yale School of Medicine's Collaboration for Regulatory Rigor, Integrity, and Transparency (CRRIT).

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Executive Summary

This report examines cases of noncompliant clinical trial results reporting obtained through Freedom of Information Act requests (FOIA) and provides evidence-based insights to strengthen enforcement methods at the FDA and NIH in clinical trial results reporting. This paper also details how Congress and Universities Allied for Essential Medicines (UAEM) have pushed for greater enforcement of clinical trial results reporting law.

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Executive Summary

Background

Provides context for the importance of transparency in clinical trial results reporting and regulatory oversight. Significant tax-payer investment in biomedical research and cases of patient harm due to obscurity in results reporting serve as clear rationale for timely and complete results reporting to ClinicalTrials.gov. Congress has been prompted by widespread noncompliance in clinical trial reporting to enact several pieces of legislation that expand public access to information regarding approved products, granting broader enforcement responsibilities to the FDA and NIH. Despite Congressional efforts to improve timely and complete clinical trial reporting, limited regulatory oversight has allowed outstanding cases of noncompliant trials to remain unaddressed.

FDAAA Enforcement and Guidance at the FDA and NIH

Offers an explanation of the unique enforcement responsibilities at the FDA and NIH for clinical trial reporting to ClinicalTrials.gov. The FDA has the authority to issue Preliminary Notices and Notices of Noncompliance to responsible parties for potential noncompliance and levy civil money penalties of up to \$10,000 per day in cases of outstanding inaction after receiving a Notice. Despite widespread underreporting, the FDA has never imposed fines on noncompliant sponsors and has only issued five Notices of Noncompliance with civil money penalty warnings. Issued Notices have been highly successful in yielding compliance. The NIH has the authority to withhold or deny grant money to responsible parties who have not met reporting standards for other studies. NIH can publish Notices on ClinicalTrials.gov for public access and can maintain a list of delinquent responsible parties (called the "Problems List"), which it may share with the FDA.

UAEM University Clinical Trials Transparency Reports (2019/2021)

Describes Universities Allied for Essential Medicines (UAEM), the non-profit health justice international organization providing the analysis for this report through its ongoing Clinical Trial Transparency campaign. In 2019, UAEM published a report investigating clinical trial compliance practices at academic research institutions. Following outreach with these universities about reporting activities, UAEM conducted a follow-up analysis and discovered improvements in results reporting at major academic research centers.

UAEM's FOIA Investigations on Agency Enforcement

Details UAEM's multi-year Freedom of Information Act (FOIA) request investigation into the FDA and NIH to examine existing enforcement activities of clinical trial results reporting. Among these FOIA requests are:

- Email communications sent by the FDA to noncompliant responsible parties, revealing extended delays between missed results submission deadlines and the issuances of Preliminary Notices of Noncompliance (Pre-Notices) and Notices of Noncompliance. The contents of the Pre-Notices produced through the FOIA request show that the FDA does not consistently share clear enforcement timeframes for trial sponsors to understand potential penalties for delayed results submissions.
- The 2023 Section 2052 report of the 21st Century Cures Act, outlines ClinicalTrials.gov oversight and compliance activities at the FDA and NIH. These documents demonstrate that the FDA and NIH are knowledgeable of widespread noncompliance. While the NIH provides clear commitments towards strengthening oversight, the FDA does not describe any intentions to increase its regulatory authority.

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HHS OIG Investigation of NIH

The OIG 2022 NIH audit found more than half of the clinical trials evaluated were noncompliant with reporting requirements. The OIG recommended that the NIH improve protocols to facilitate timely results reporting and take enforcement actions against noncompliant sponsors. Four Congressmen, Senators Marsha Blackburn, Charles Grassley, Ron Johnson, and Roger Marshall, sent a letter to the NIH demanding the agency provide a response as to how it will address outstanding noncompliance discovered in the OIG audit. UAEM filed a FOIA request for the NIH's response to these congressmen, wherein the agency commits to strengthening ClinicalTrials.gov evaluation mechanisms.

Engagement with the United States House Committee on Energy and Commerce

In January 2023, Ranking Member of the House Energy and Commerce Committee Frank Pallone partnered with UAEM to write a letter to the FDA and NIH inquiring about noncompliance in results reporting. In April 2023, the FDA and NIH provided an interagency response discussing the effectiveness of current regulatory efforts and steps to address outstanding noncompliance. The FDA made no commitment towards increasing the issuance of Notices and wrote that failure to comply with reporting requirements would not prevent licensing, approval, or clearing of marketing applications. However, the NIH presented a stronger commitment to enforcement, outlining actionable steps taken to monitor cases of noncompliance through developing new guidance on enforcement of results reporting and potentially withholding grants from responsible parties who fail to meet reporting requirements.

UAEM's Citizen Petition to the FDA

Defines the scope of the FDA Citizen Petition filed by Columbia Law School's Science, Health, and Information Clinic on behalf of UAEM in February 2023. The petition uses evidence-based insights to request that the FDA take the following actions to strengthen the oversight of clinical trial results reporting:

1. Increase the issuance of Notices to noncompliant responsible parties and impose civil money penalties where appropriate.
2. Utilize a prioritization framework to emphasize enforcement for products without proven alternatives, trials intended to address public health emergencies, and trials that focus on diseases that disproportionately impact marginalized communities. The FDA should also allocate resources to monitor the compliance of responsible parties and those who have a history of noncompliance.
3. Establish a public dashboard of all Preliminary Notices of Noncompliance (Pre-Notices) issued to responsible parties.

The FDA was federally required to respond to the Citizen Petition by August 26th, 2023, however, the agency issued an interim response two days prior to the deadline citing it "will require additional time to issue its final response to [the] petition..."¹

In response, UAEM worked with Congressman Neal Dunn to write a letter to the FDA Commissioner specifically recommending that the FDA implement the enforcement actions outlined within UAEM's Citizen Petition. The FDA replied in a letter to Congressman Dunn, acknowledging the agency had not fully responded to UAEM's Citizen Petition at the time, without making a commitment to implementing UAEM's requests.

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Within a week of responding to Congressman Dunn, the FDA implemented one of UAEM's requests in the Citizen Petition by launching a public dashboard of issued Pre-Notice letters to noncompliant responsible parties.

The FDA provided a complete response to UAEM's Citizen Petition on February 21, 2024, with the following:

- 1. Denied**– The FDA refuses to increase its enforcement efforts. It claims, among other things, that voluntary compliance is enough: “As in all areas that FDA regulates, the Agency’s goal is to achieve timely voluntary compliance with the law without having to resort to legal action, which can be resource-intensive and time-consuming.”
- 2. Partially Granted**– The FDA denied UAEM's request to issue new guidance for its enforcement efforts. However, the agency granted UAEM's request that the FDA consider UAEM's proposed enforcement framework if and when the FDA decides to revise existing guidance.
- 3. Granted**– The FDA granted UAEM's request to establish a dashboard of previously issued Pre-Notices. The agency executed this request by launching the dashboard on December 4, 2023. The FDA has committed itself to adding newly issued Pre-Notices on a quarterly basis. The FDA agreed with UAEM's arguments about the value of transparency: “We believe that public availability of Pre-Notice letters will provide greater transparency and awareness of FDA's compliance actions and may further increase voluntary compliance by responsible parties.”

UAEM's success in urging the FDA to launch a Pre-Notice dashboard marks a significant step forward in addressing accountability for noncompliant responsible parties. However, the FDA's refusal to increase enforcement initiatives demonstrates that the agency is unaware of the impact of ClinicalTrials.gov on patient health outcomes.

Insights and Recommendations

Examines several factors that contribute to ongoing noncompliance with FDAAA and offers a series of interventional evidence-based enforcement recommendations.

- **Lack of coordination** between the FDA and NIH serves as a significant barrier to ClinicalTrials.gov reporting management. This analysis reveals minimal enforcement and data-sharing between the FDA and NIH.
- There are also **no instances where noncompliant intramural NIH trials received Pre-Notices from the FDA**. Despite several staff members and reports demonstrating that the FDA and NIH are knowledgeable of noncompliance with FDAAA, there has been limited enforcement efforts and no fines to responsible parties.
- While limited in number, **Notices have proven highly effective in increasing compliance**, yet the FDA has not established an automated notification system. The FDA has also cited funding as a barrier to resource allocation for ClinicalTrials.gov enforcement.
- UAEM provides an analysis of the FDA's funding, demonstrating how the FDA places greater resources towards drug approvals rather than regulatory processes that receive fewer appropriations. As such, UAEM recommends that the FDA increase the issuance of Pre-Notices, clarify enforcement timelines in Pre-Notices, and request additional budget authority for ClinicalTrials.gov oversight.

Why is Clinical Trials Transparency Important?

Over the past two decades, the role of clinical trial data in scientific investigations has transformed the legal and ethical impact of biomedical research. In 2023, Congress allocated \$54 billion for biomedical research, including more than \$47.5 billion to the National Institutes of Health (NIH), 85% of which is granted to universities and laboratories operating outside of the agency's institutes themselves.^{2,3} The clinical trial data produced through this public investment is an essential public good, as access to this data informs doctors and patients of valuable treatments, protects the public from treatments that may be predicated on incorrect data, and holds the FDA and researchers accountable to report accurate and timely data.

Clinical trial data opacity has directly harmed patient health when a product reaches the market without data to validate the advertised effects. In the early 2000s, producers of the influenza antiviral FDA-approved drug Oseltamivir (Tamiflu ®) withheld results of adverse side effects.⁴ Despite recommendations from key health officials in Japan and researchers at Oxford, undisclosed trial results prompted continued distribution and stockpiling of the drug in the U.S. and globally.^{5,6} **Several studies later identified the incidence of adverse events in pediatric patients prescribed Tamiflu such as hepatitis, neuropsychiatric events, cardiac arrhythmia, and skin hypersensitivity reactions.**⁷

Transparency in clinical trials is also important for regulators who are responsible for overseeing the ethical stewardship of taxpayer investments. The Tamiflu disaster revealed that delays or omissions in results reporting can not only harm patients but also waste billions in taxpayer dollars.

Researchers at the Indian Journal of Pharmacology documented that the "U.S. had spent more than \$1.3 billion developing and stockpiling 65 million treatments... of Tamiflu alone. Across the globe, over \$20 billion in public money has been spent on stockpiling Tamiflu and Relenza."⁸

Tamiflu is not an entirely unique case. One study found that the median reporting time for an applicable clinical trial was just under one year after the reporting deadline.⁹ Regulators must consider how these delays and underreported clinical trial data contribute to adverse health outcomes and waste taxpayer dollars when determining the efficacy of enforcement practices.

ClinicalTrials.gov and the FDA Amendments Act of 2007

In the early years of Tamiflu distribution, drug regulation was far behind the rapidly developing drug industry. The Food and Drug Administration Modernization Act of 1997 (FDAMA) required the NIH gather information not only on trial registration but also on trial design and results.¹⁰ The NIH was also required to establish a public information database for results reporting. Pursuant to FDAMA, in February 2000 the National Library of Medicine at the NIH established ClinicalTrials.gov, a public-facing resource for trial data regulated by the FDA.¹¹ This was the first step toward realizing the aims of FDAMA and allowing regulation to keep pace with innovation. However, FDAMA did not afford the FDA or NIH significant enforcement mechanisms to create compliance around results reported to ClinicalTrials.gov.

Tamiflu is not the only case where clinical trial under-reporting caused patient harm. In 1999, Merck started to market the drug Vioxx as a new painkiller. In advertisements featuring world figure skating champion Dorothy Hamill, Merck claims "with one little pill a day, Vioxx can provide 24 hours of relief."¹²

Vioxx resulted in \$11 billion in profits between mid-1999 and 2004. Meanwhile, the drug company did not disclose adverse cardiovascular events, resulting in the deaths of 38,000 people across the United States.^{13, 14} Following Merck's over \$4.8 billion Vioxx settlement fund, Congress decided to require stronger reporting and enforcement regulations.

In 2007, Congress enacted the FDA Amendments Act (FDAAA), which mandated public reporting of the results of essentially all late-stage clinical trials of FDA-regulated drugs and devices to ClinicalTrials.gov for review and approval by the FDA. More specifically, section 801 of FDAAA, which is codified in section 402(j) of the Public Health Service (PHS) Act, requires the responsible party of applicable clinical trials (ACTs) to submit trial summary results and adverse events information to ClinicalTrials.gov within 12 months of the trial's primary completion date. FDAAA also establishes monetary penalties for responsible parties who fail to comply of up to \$10,000 per day and potential criminal liability.¹⁵ The NIH and FDA share the responsibility of enforcing FDAAA, yet minimal oversight from both agencies has resulted in over **4,000 clinical trials missing results on ClinicalTrials.gov**.¹⁶ The FDA Commissioner, Robert M. Califf, has warned that missing results from ClinicalTrials.gov could distort the medical literature: "[I]ncomplete reporting of studies sponsored by academic medical centers shows similar biases, including lack of publication of substantial proportions of studies and selective outcome and adverse event reporting."¹⁷ Commissioner Califf's remarks reflect the issue of widespread noncompliance and the need to strengthen enforcement.

The Final Rule

In 2016, the U.S. Department of Health and Human Services (HHS) and the NIH issued 42 CFR Part 11, the *Final Rule for Clinical Trials Registration and Results Information Submission*.¹⁸ The final rule implements provisions from section 402 (j) of the Public Health Services Act (PHS Act) to enforce FDAAA section 801. Under the new provision, the Secretary of Health and Human Services is mandated to use rulemaking to improve public access to information on ClinicalTrials.gov. The final rule also created structured criteria to determine which studies are considered to meet the definition of an Applicable Clinical Trial.¹⁹

The final rule also required that trial sponsors designate one responsible party for submitting results to ClinicalTrials.gov along with the submission of results information for unapproved products. The final rule became effective on January 18, 2017, with responsible parties expected to become compliant by April 18, 2017. This legislation is significant because it increases accountability for trial reporting and clarifies which trials must be reported to ClinicalTrials.gov. As such, the FDA should be able to efficiently streamline enforcement by identifying which trials qualify as Applicable Clinical Trials and notifying a single representative regarding the status of missing results.

The FDA and NIH's Roles in Enforcing FDAAA and the Final Rule

Congress gave HHS the responsibility to oversee compliance with FDAAA and to punish noncompliant responsible parties through withholding grant funds, levying civil money penalties, and recommending criminal prosecution.²⁰ The Secretary of the HHS delegated this enforcement responsibility to the FDA Commissioner. Compliance with ClinicalTrials.gov today relies on the FDA's oversight.²¹

The FDA also coordinates enforcement with the NIH by communicating which responsible parties have received results reporting violation letters known as Notices of Noncompliance. The NIH publishes these Notices on ClinicalTrials.gov for public access and maintains a list of noncompliant trial sponsors which it may share with the FDA.²²

Although the NIH has independent authority and obligations under FDAAA to withhold grant money from grantees who fail to comply, the NIH has only withheld grant money in two instances. Additionally, the NIH has publicly declared that trials without NIH support are not under their jurisdiction, and instead are under the FDA's.²³ If enforced, these regulatory efforts would prevent research duplication, scientific fraud, and ultimately ensure public access to trial results.

The FDA's 2020 Enforcement Guidance

The FDA issued guidance in 2020 relating to how the agency exercises its FDAAA enforcement authority in cases of noncompliant responsible parties.²⁴ This guidance stipulates that the FDA identifies and investigates noncompliance through the agency's Bioresearch Monitoring (BIMO) program. Evidence gathered for these investigations is obtained either privately, through direct complaints made to the FDA about a particular clinical trial, or by reviewing complaints made publicly. As a result of these investigations, the FDA may issue a Preliminary Notice of Noncompliance ("Pre-Notice") to noncompliant responsible parties who failed to register an applicable clinical trial, failed to submit required clinical trial information, or submitted false or misleading clinical trial information. If a responsible party does not reply to a Pre-Notice within 30 days, the FDA can initiate an investigation to determine the significance of the violation.²⁵

Criteria for judging the significance of a violation:

- (1)** Responsible parties of applicable clinical trials whose products pose potentially serious effects to trials subjects and the public
- (2)** Responsible parties who have shown a repeated consistent pattern of noncompliance
- (3)** A violation exists in conjunction with other statutory or regulatory violations

In cases where a violation is substantial, the FDA may issue a Notice of Noncompliance to inform the sponsor that the FDA may, after 30 days of issuing the Notice, seek fines of up to \$10,000 per day if the sponsor is deemed to be noncompliant.

To date, the FDA has neglected to collect any of the existing \$46 billion dollars it is due in noncompliance fines, and has only issued 149 Pre-Notices and five Notices of Noncompliance since FDAAA legislation came into effect. HHS can also recommend that the FDA pursue criminal prosecution of noncompliant responsible parties.²⁶

UAEM University Clinical Trials Transparency Reports

In 2019, Universities Allied for Essential Medicines (UAEM) conducted a transparency report on the state of clinical trial reporting by 40 leading U.S. universities.²⁷ This report identified that 27 of the top 40 research universities violated reporting requirements under FDAAA. Results from 140 clinical trials from the cohort studied, or 31% of trials conducted by universities since 2017, were missing from ClinicalTrials.gov.

In a follow-up analysis conducted in 2021, UAEM found that legal compliance at universities had tremendously increased, finding institutions with robust clinical trial programs achieving 100% compliance. Columbia University and Northwestern University serve as positive examples of growth, improving from respective rates of 16.7% and 30% in 2019 to 100% in 2021.²⁸

Public pressure and broader federal oversight are effective mechanisms for improving compliance. This is evidenced by the fact that reporting improvements came shortly after UAEM's report and a December 2018 lawsuit filed by the Yale Media Freedom and Information Access Clinic against the FDA, NIH, and HHS on behalf of medical researchers Charles Seife and Peter Lurie.²⁹ The lawsuit, which was informed by UAEM's 2019 report, challenged a 2016 decision by the HHS that allowed trials conducted between 2007 and 2017 and completed prior to FDA approval for a product to not report results. A federal judge ruled that required results be posted to ClinicalTrials.gov, thus reversing the HHS decision. Subsequent improvements in university reporting compliance in UAEM's 2021 report demonstrate that institutions can effectively improve their trial reporting compliance in a short time frame.

UAEM's FOIA Investigations on Agency Enforcement

In 2007, Congress designated the FDA as the responsible agency for issuing civil money penalties under FDAAA Section 801. However, the first public example of the FDA threatening to levy fines did not come until 14 years later. In 2021, the FDA issued its first Notice of Noncompliance to Acceleron, which caused the NIH to input a public notice of "FDAAA 801 Violation" into the ClinicalTrials.gov entry for the trial. Notices of Noncompliance are one of the only metrics available to the public to evaluate clinical trials that are missing required results information and the FDA's enforcement. As a result of limited public information about the FDA exercising enforcement authority and subsequent compliance trends, UAEM pursued multiple Freedom of Information Act (FOIA) requests with the FDA and NIH to evaluate the extent of regulatory oversight and responsible party compliance.

UAEM's 2021 FOIA Investigation

Columbia Law School's Science Health and Information Clinic (SHIC) filed FOIA requests on behalf of UAEM in March 2021, requesting "all records – including emails and memoranda – documenting FDA's investigations of responsible parties who, within 30 calendar days of receiving a Pre-Notice Letter, fail to address the potential FDAAA violations described in such Pre-Notice Letter."³⁰ The FDA released a series of Pre-Notices that had been issued to noncompliant responsible parties, but the agency did not provide any email communications. From 2013 through April 2021, the FDA issued 57 Pre-Notices.³¹ More than 90% of the Pre-Notice recipients reported missing information shortly after the notices were sent. Documents produced through this investigation indicate that the NIH is also aware that Pre-Notices are very effective and generate quick compliance from responsible parties. Additionally, the NIH, National Library of Medicine (NLM), and FDA cooperated to create templates for Pre-Notice and Notice letters, demonstrating that interagency cooperation is indeed possible.³² At the time the FOIA documents were generated, four responsible parties who had failed to submit results after receiving an initial Pre-Notice, became compliant after receiving a Notice of Noncompliance.

2052 Report

In 2016, Congress passed section 2052 of the 21st Century Cures Act to address noncompliance with FDAAA and minimal regulatory oversight. Section 2052 requires the Secretary of the Department of Health and Human Services (HHS) to coordinate with the FDA Commissioner and Director of the NIH to provide a “Report on Activities To Encourage Compliance” related to ClinicalTrials.gov oversight.³³ Section 2052 stipulates that both the NIH and FDA issue reports every two years, for a total of four years, on enforcement activities. The result has been three reports between 2019 and 2023.³⁴

The NIH provided UAEM with the 2023 Section 2052 report, following an April 2023 FOIA request.³⁵ The report revealed that the NIH collected data on trial results that were submitted on time, submitted but not reviewed, and for trials that delayed the submission date.³⁶ The table (Table 1) did not include a column for trials that missed their deadline and had not legally delayed their submission data through a Good Cause Extension which “demonstrates good cause for the extension and provides an estimate of the date on which the information will be submitted.”³⁷ However, subtracting the number of trials that submitted or delayed their results from the total number of trials reveals that reporting results for 284 out of 955 trials were late or otherwise unaccounted for. **This data demonstrates that the NIH is knowledgeable of noncompliance with results reporting.**

VII. Table 2. Total Number of Registered ACTs with Summary Results Information Submitted to ClinicalTrials.gov: January 18, 2017–September 30, 2022

ACT Results Status**	FY 2017†	FY 2018	FY 2019	FY 2020	FY 2021	FY 2022
ACTs that reached the standard results submission deadline	0	139	963	1,999	2,512	2,851
Results submitted and posted (QC review concluded)	0	92	692	1,378	1,484	1,155
Results submitted (QC review not yet concluded)^	0	10	55	124	183	349
Submission deadline delayed^	0	2	16	39	149	182

In the FDA's response, the agency shared that between October 1, 2020, and September 30, 2022, the FDA's BIMO had conducted 187 inspections of sponsors to investigate ClinicalTrials.gov compliance. However, the FDA shared that during the same timeframe, only 52 Pre-Notice letters were issued to noncompliant sponsors. The agency made no reference to the compliance status nor to the enforcement mechanisms taken in the other 135 cases investigated. Section 2052 reports provide valuable information about ongoing enforcement practices at the NIH and FDA. Despite outstanding cases of noncompliance in clinical trial reporting, Congress has not reauthorized 2052 reporting beyond 2023.

UAEM's 2023 FOIA Analysis Reveals Scope of Clinical Trial Noncompliance and Areas for Strengthening the FDA's Enforcement Systems

In March 2023, UAEM requested a status update on its March 2021 FOIA request for email communications and Pre-Notices issued to noncompliant responsible parties, given the FDA had not responded to the full request. The FDA shared additional documents on May 25, October 18, and November 1, 2023. These documents encompass a total of 32 noncompliant responsible parties involved in email communications with the FDA dated between July 2020 and March 2023.³⁸ The contents of the emails detail how noncompliant responsible parties responded to outstanding issues in results submissions and the quality review process.

Analysis of the data from the provided FOIA responses reveals the following insights:

Table 2: Timelines for FDA Enforcement and Resulting Sponsor Compliance

Category	Median (Days)	Interquartile Range (Days)*
Time after Reporting Deadline Until Pre-Notice is Issued	497	289
Time After First Pre-Notice Letter Until Sponsor Replied	48	51
Time After Pre-Notice Issued Until Sponsor Updates ClinicalTrials.gov	89	173
Time between Pre-Notice and Notice of Noncompliance	278	40.75
Time for Sponsor to Reply to Notice of Noncompliance	2	3
Time After Notice of Noncompliance that Sponsor Updates ClinicalTrials.gov	5.5	11.75

*Interquartile Range measures the spread of the data for the middle half of a data set

Positive Correlation between Timeliness of FDA Pre-Notice and Sponsor Reporting Compliance

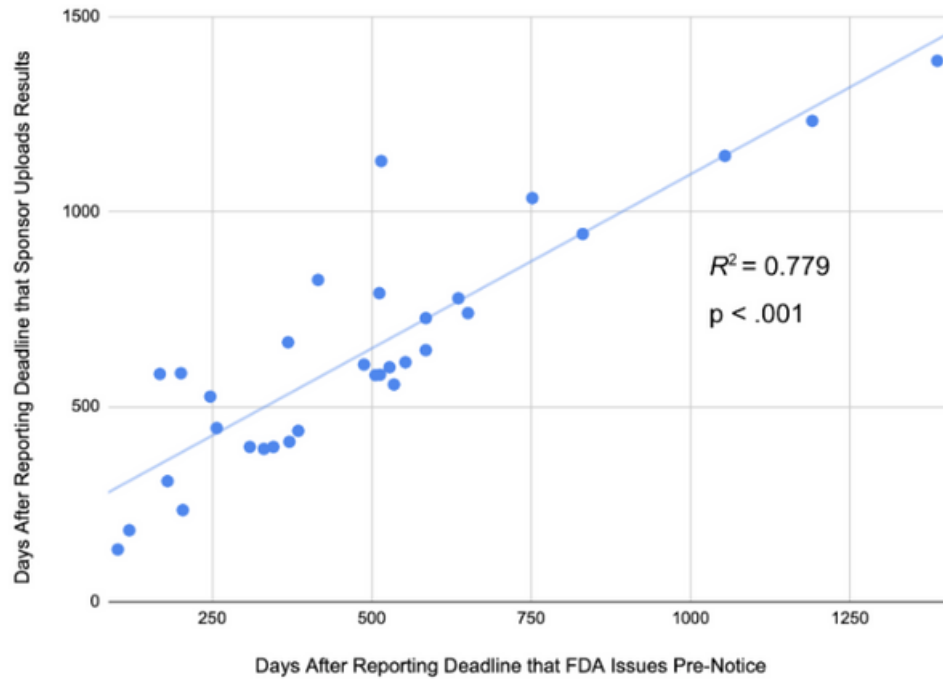


Figure 2. This figure demonstrates a strong positive correlation ($R = 0.882$) between the time for the FDA to issue Pre-Notices following missed results reporting deadlines and the time for sponsors to submit missing results to the Protocol Registration and Results System. The p-value ($2.382e-11$, $<.001$) is statistically significant and shows that Pre-Notices are effective in increasing compliance with results-reporting regulations.

The short average response time between receiving a Notice of Noncompliance and updating ClinicalTrials.gov underscores the sponsors' urgency and commitment to addressing official escalations. This data also shows that Pre-Notices can improve clinical trial transparency compliance effectively. Moreover, these findings demonstrate the effectiveness of Notices of Noncompliance to increase results reporting. To this end, timely monitoring and communication between the FDA and sponsors is paramount to ensure compliance and prompt resolution of discrepancies.

This review also identified issues in the Protocol Registration and Results System (PRS), a website that responsible parties use when submitting results for the FDA's quality control review process. Responsible parties are required to submit results to the PRS within 12 months from the study's primary completion date, which is "the date that the final participant was examined or received an intervention for the purposes of final collection of data for the primary outcome."³⁹ As stated above, responsible parties may submit a Good Cause Extension request for delaying results reporting to the PRS with a justifiable explanation for delayed reporting along with a new estimated submission date.

UAEM's Clinical Trial Transparency Campaign and FOIA Investigation

Nevertheless, when sponsors broke the final rule and submitted certifications for delayed submission of results past their standard submission deadline, the PRS failed to provide new result due dates and the sponsors were not penalized for their inaction.⁴⁰ In a November 2020 letter, the FDA informed a sponsor of the PRS issues,

"Please note that although the National Library of Medicine's ClinicalTrials.gov Protocol Registration and Results System (PRS) permits you to submit a certification for delayed submission of results and provides a new expected results due date in the study record, such certification is only timely when submitted 'prior to the results information submission deadline.' PRS staff are in the process of modifying the PRS to address this issue."⁴¹

While the agency stated it would work to address the issue, this incident emphasizes the need for improved systems that can evaluate and regulate submission modifications.

Responsible parties have cited concerns regarding the ambiguity of guidance in the FDA's Pre-Notice letters. In Pre-Notices, the agency requests the responsible party "promptly" submit missing results. In one correspondence, a sponsor detailed how it would process results two months after receiving a Pre-Notice and asked "Is this an acceptable timeline that would meet the definition of 'promptly'?" This correspondence is a clear indication that sponsors and responsible parties are looking to the FDA to set clearer terms of compliance. In the absence of enforced deadlines, responsible parties are neither held accountable nor are they incentivized to submit results in a timely manner. While the FDA included warnings of civil money penalties in a handful of letters, this language was inconsistently included across the Pre-Notices evaluated. Nevertheless, no responsible party has ever received a civil money penalty despite noncompliance.

Responsible parties have also actively limited results dissemination to the public. In one of the FDA's FOIA productions, a representative from First Wave Biopharma explicitly forbade the FDA from releasing correspondence that the company was federally mandated to submit. First Wave stated in its letter, **"We consider the information contained in this letter...not subject to disclosure under the Freedom of Information Act."** While section (b)(4) of the Freedom of Information Act, "allows the United States to withhold from disclosure trade secrets...obtained from a person that is privileged or confidential," the Office of Federal Contract Compliance Programs will ultimately determine whether this exemption is warranted.⁴² This request is evidence that responsible parties want certain information withheld from the public and indicates resistance to transparency in results reporting.

On August 12, 2022, the Department of Health and Human Services Office of Inspector General (OIG) published a report examining to what extent the NIH took enforcement efforts to ensure NIH-funded intramural trials (conducted by the NIH) and extramural trials (conducted outside of the NIH) were compliant with federal reporting requirements. The OIG reviewed reporting deadline adherence across 72 NIH-funded intramural and extramural clinical trials that were mandated to report results in 2019 and 2020. The audit also investigated whether NIH posted submitted results to ClinicalTrials.gov within 30 days of receiving them.

The OIG found that over half of the clinical trials evaluated were noncompliant with reporting requirements. Noncompliant trials either failed to submit results or submitted results after the federal deadline.

Table: Summary of Clinical Trials Requiring Results To Be Submitted in 2019 or 2020

	Intramural	Extramural	Total
Submitted on Time	20	15	35
Submitted Late	11	1	12
Results Not Submitted	5	20	25
Subtotal of Noncompliance	16	21	37
Total	36	36	72

While the OIG found that the NIH complied with posting results to ClinicalTrials.gov within 30 days from the submission date, the report attributes reporting deficiencies to inadequate enforcement procedures in all other aspects. The NIH ineffectively ensured reporting and funded additional research endeavors for responsible parties who had failed to report results for other clinical trials, although the NIH has the authority to withhold funding from responsible parties who failed to report results.

The OIG recommended that the NIH improve protocols to facilitate timely results reporting and take enforcement actions against noncompliant sponsors who are late in reporting results or do not report results. The OIG also encouraged the NIH to help responsible parties understand submission guidelines for ClinicalTrials.gov.

The NIH submitted written comments to the OIG concurring with the recommendations set forth in the OIG’s audit. The NIH shared with OIG that the agency was aware of responsible parties facing challenges in results reporting. Furthermore, the NIH committed to investing in improvements to ClinicalTrials.gov accessibility and increasing compliance actions against responsible parties with late or missing results.⁴³

Senate Letter to the NIH

In December 2022, UAEM filed a FOIA request with the HHS to access the NIH's response to a letter sent from Senators Marsha Blackburn, Charles Grassley, Ron Johnson, and Roger Marshall to the NIH on October 13, 2022. The congressional letter inquired about the recent findings from the August 2022 OIG investigation of the NIH's enforcement of clinical trial results reporting. The senators wrote:

"When American taxpayers spend billions of dollars on federal programs, they expect accountability, transparency, and results. HHS OIG's report makes clear that the NIH must do more to hold grant recipients accountable." ⁴⁴

The letter continued with several questions about the scope of the NIH's oversight and plans to address enforcement concerns cited in the OIG report.

Response from the NIH and Commitments to Improving Clinical Trial Oversight

The HHS provided UAEM with the NIH's response to the four congressmen on January 20, 2023.⁴⁵ The NIH response dated December 20, 2022, described the agency's efforts to advance oversight for both intramural and extramural research. The NIH defined responsibilities and procedures for reporting intramural clinical trials and established procedures for addressing noncompliance in the NIH Policy Manual. For extramural trial regulation, the NIH developed a "Clinical Trials Compliance Workflow" with modifications to the electronic Research Administration (eRA) systems to alert NIH staff of clinical trial registration, cases of potential noncompliance, and late registration or results reporting. The NIH also implemented a system screen to ensure no awards are issued without "resolving delinquent registrations or results reporting." These actions demonstrate that the OIG investigation and Congressional pressure prompted the NIH to make a commitment to developing and sustaining improvements in enforcement that will support transparency in clinical trial results reporting.

Ranking Member Frank Pallone, the U.S. House Energy and Commerce Committee sends letter to the FDA and NIH on UAEM's Behalf

On January 19, 2023, Representative Frank Pallone, who is the Ranking Member of the House Committee on Energy and Commerce, wrote a letter to the FDA Commissioner Robert Califf and NIH Director Lawrence Tabak. In his letter, Representative Pallone raised concerns regarding the growing issue of responsible parties failing to submit timely results and requested information pertaining to enforcement actions taken by both the FDA and the NIH to address noncompliance related to FDAAA.

Response from the FDA and NIH

On April 11, 2023, the FDA and NIH issued a formal response to Representative Pallone, which UAEM received via a FOIA request.⁴⁶ This letter described how, as of February 14, 2023, the FDA had issued 92 Pre-Notice letters. The agency described this enforcement method as being “largely effective in securing compliance” with over 90% of Pre-Notice letter recipients and 100% of Notice of Noncompliance recipients submitting required information.

Despite the efficacy of Pre-Notices and Notices of Noncompliance, the FDA did not commit to issuing more letters.

Instead, the FDA maintained that the issue of results reporting was a lesser priority when compared to “other components of FDA’s BIMO program that may have greater and more direct public health impact.”

The FDA also noted that failure to comply with reporting requirements would not prevent the approval, licensing, or clearing of marketing applications. However, the Public Health Service Act 45 C.F.R. Part 11, clearly requires results reporting compliance prior to clearing marketing applications.

The FDA shared that it uses a combination of an internal analytics program that incorporates ClinicalTrials.gov data and subsequent staff review to assess sponsor compliance with ClinicalTrials.gov. The FDA asserted that this methodology had found a “very high level of compliance during inspections,” despite the fact that over 20% of trials are missing results from the database.^{47,48} The agency went on to say it utilizes a risk-based prioritization framework to determine when to issue Notices of Noncompliance.

The FDA's risk-based framework includes the following criteria:

- Vulnerability of the population under study
- Nature and novelty of the product involved in the trial
- If the product involved is intended to address a significant public health need
- Risks to trial participants
- If the product involved is approved/unapproved
- Whether ClinicalTrials.gov noncompliance exists alongside noncompliance with other statutory or regulatory requirements
- Whether the trial required submission of an IDE (investigational device exemption) or IND (investigational new drug) application

Despite the existence of this risk-based prioritization framework, the FDA has failed to rigorously apply it. Many noncompliant trials fit the above criteria but have not received a Notice of Noncompliance. This was evident in UAEM's FOIA investigation, which identified that out of the 32 cases of Notice recipients, only 22% of the Notices issued followed the risk-based criteria.

While the FDA cited limited funding as a barrier to enforcement, it continues to employ ineffective manual surveillance methods as compared to the NIH. To this end, the NIH utilizes an automated quarterly report to identify potential noncompliance of responsible parties.⁴⁹ The differences in enforcement tactics between the two agencies are likely to account for the NIH's issuance of 317 potential noncompliance letters compared to the FDA's 92 Pre-Notice of Noncompliance letters as of February 2023. In light of the FDA's limited resources, it is critical that the agency invests in efforts to automate and increase oversight.

In the NIH's response to Representative Pallone, the agency provided a stronger commitment to improving oversight of ClinicalTrials.gov. While the FDA maintains in its letter that results reporting oversight may be a lesser priority, the NIH claims that it "takes its responsibilities in facilitating compliance with these requirements seriously." The NIH has taken measurable steps toward this commitment. In April 2023, the NIH followed through on its statement to Representative Pallone that the agency would be placing "holds on current funding or withholding of future funding" by withholding approval of new research for two principal investigators who had not reported trial results within one year of the primary completion date.⁵⁰ Moreover, the NIH's Intramural Research Program (IRP) developed and published the NIH Policy Manual Chapter 3007 (MC 3007) containing "Clinical Trial Registration and Results Information Reporting" in January 2022. This chapter establishes responsibilities for reporting and consequences in the event of noncompliance. The agency asserts that this new program has proven a successful tool to facilitate intramural compliance with reporting requirements.

UAEM's Citizen Petition to the FDA

On February 27, 2023, Columbia Law School's Science, Health, and Information Clinic (SHIC), filed an FDA Citizen Petition on behalf of UAEM under docket number FDA-2023-P-0660.⁵¹ Citizen petitions enable the American public, including UAEM, to directly request that government agencies take recommended administrative actions.⁵² UAEM filed the petition with the FDA to provide evidence-based insights that prioritize patient health and safety amid outstanding reporting deficiencies and noncompliance with FDAAA.

The petition aims to increase FDA enforcement of clinical trial results reporting requirements by:

1. Increasing the issuance of Pre-Notices to a minimum of 250 Notices per year and imposing civil money penalties when appropriate.
2. Utilizing a prioritization framework: a detailed, organized, and hierarchical list of enforcement priorities explaining how the FDA should enforce requirements in both pivotal and non-pivotal trials. Pivotal trials provide the basis for the FDA's decision to approve a drug.⁵³ Non-pivotal trials do not directly determine the FDA's decision for approvals, yet provide additional information that can potentially reveal safety problems. Moreover, data from both pivotal and non-pivotal trials offer important findings about approved products and should therefore be accessible to patients. The proposed prioritization framework would also place greater importance on trials involving responsible parties or sponsors with a specific pattern of previous noncompliance. Finally, prioritization should focus on trials with no proven alternative treatments, trials intended to address public health emergencies, and trials pertaining to diseases with a disproportionate impact on marginalized populations.
3. Creating a publicly available dashboard containing all Pre-Notices sent to potentially noncompliant parties responsible for reporting clinical trial results. This would ensure that the public and responsible actors have access to information, given that the FDA had not published information about when and to whom it issues Pre-Notices.

Interim Response from the FDA

The FDA was federally required to respond to UAEM's Citizen Petition on August 26, 2023, 180 days after the petition was filed. However, the agency issued a non-substantive response only two days prior to the deadline, citing it "will require additional time to issue its final response to [the] petition...."⁵⁴ The FDA's decision to forgo a timely formal response to the items in UAEM's petition suggests that the agency prioritizes neither transparency in clinical trials nor timely results reporting.

Congressman Neal Dunn Sends letter to the FDA to support requests in the UAEM Citizen Petition

On September 29, 2023, Congressman Neal Dunn wrote in support of UAEM's Citizen Petition following the FDA's interim response.⁵⁵ Congressman Dunn requested that the FDA respond in full to UAEM's Citizen Petition and implement the recommendations for improving trial results reporting. Congressman Dunn's letter emphasized the enactment of UAEM's Citizen Petition requests: (1) increase the issuance of Pre-Notice letters and Notices of Noncompliance, (2) draft new guidance documents for how the FDA will materially improve enforcement efforts, and implement the prioritization framework for publicly funded trials, and (3) create a public dashboard for all Pre-Notices submitted to responsible parties and routinely update this dashboard with all changes and updates as necessary.

The FDA Responds to Congressman Dunn and Launches Pre-Notice Dashboard

On November 30, 2023, the FDA responded to Congressman Dunn, highlighting that it "...supports and shares the goal of increasing transparency of information about clinical trials through ClinicalTrials.gov" and "is always looking at ways to refine its processes for identifying potential noncompliance and issuing Pre-Notice Letters and Notices of Noncompliance." The FDA also acknowledged that it had not substantively responded to the Citizen Petition, but understood that implementation of its recommendations could increase compliance with federal statutes and protect patient and public health.

Shortly thereafter the FDA implemented one of the requests in UAEM's Citizen Petition by launching the first publicly available dashboard for issued Pre-Notice letters on December 4, 2023.⁵⁶ This move demonstrates that the FDA is capable of incorporating some of the requests provided in the Citizen Petition and suggests the FDA may be considering other methods to strengthen the enforcement of clinical trial results reporting.

The FDA Responds to UAEM's Citizen Petition

The FDA provided a complete response to UAEM's Citizen Petition on February 21, 2024, with the following:

1. Denied– The FDA refused to increase its enforcement efforts. The agency claimed, among other things, that voluntary compliance is enough: “As in all areas that FDA regulates, the Agency’s goal is to achieve timely voluntary compliance with the law without having to resort to legal action, which can be resource-intensive and time-consuming.”
2. Partially Granted– The FDA denied UAEM’s request to issue new guidance for its enforcement efforts. However, the agency granted UAEM’s request that the FDA consider UAEM’s proposed enforcement framework if and when the FDA decides to revise existing guidance.
3. Granted– The FDA granted UAEM’s request to establish a dashboard of previously issued Pre-Notices. The agency executed this request by launching the dashboard on December 4, 2023.⁴⁵ The FDA has committed itself to adding newly issued Pre-Notices on a quarterly basis. The FDA agreed with UAEM’s arguments about the value of transparency: “We believe that public availability of Pre-Notice letters will provide greater transparency and awareness of FDA’s compliance actions and may further increase voluntary compliance by responsible parties.”

Although the availability of Pre-Notice letters through the dashboard is a promising method to hold noncompliant responsible parties accountable, it also highlights the limited enforcement the FDA has undertaken to effectively address the ongoing public health harms of widespread underreporting of clinical trials. The FDA has only issued 149 Pre-Notices according to the dashboard, despite thousands of clinical trials being noncompliant with the federal law that requires timely reporting of results.⁴⁵

The FDA defends its reliance on voluntary compliance, suggesting enforcement of ClinicalTrials.gov is a lesser priority:

“When deciding where to focus limited compliance resources, FDA considers which activities are likely to have the greatest and most direct public health impact and balances resource allocation to ClinicalTrials.gov with resource needs for other compliance programs...”

UAEM's Citizen Petition to the FDA

The FDA's response diminishes the value of timely and complete results reporting to ClinicalTrials.gov. The FDA further explains its decision to deny additional enforcement actions by downplaying the essential role of ClinicalTrials.gov, **"It is generally not possible to draw conclusions about the safety or efficacy of FDA-regulated medical products based solely on the limited amount of public information on ClinicalTrials.gov for any specific trial."**

This response demonstrates that the FDA is unaware of the value of ClinicalTrials.gov in determining physician prescribing practices and patient health outcomes. Moreover, the FDA's perception of ClinicalTrials.gov as a non-vital resource for the medical community justifies ongoing noncompliance with FDAAA and nondisclosure of potentially harmful side effects. The FDA's claim that data is limited on ClinicalTrials.gov also suggests that the agency should collaborate with the NIH to consider methods to improve data requirements on ClinicalTrials.gov that strengthen the reliability of information available to physicians and patients.

Problems

1. Lack of Coordination between the FDA and NIH

Coordination between the FDA and NIH is essential for ensuring proper compliance and a comprehensive ClinicalTrials.gov database. The FDA and NIH do not rely on a consistent, shared framework of enforcement, and they have not recently cooperated for Pre-Notices and Notices of Noncompliance. As of February 2023, the NIH had sent 225 more Notices than the FDA, despite the fact that the NIH funds only a small subset of the trials under the FDA's oversight that are subject to statutory reporting requirements. These letters are not sent conjunctively with the FDA, even though the FDA has greater enforcement responsibilities than the NIH. **Perhaps more significantly, the NIH and FDA do not sufficiently participate in data-sharing or communication on enforcement of certain trials or sponsors.** The FDA sent no Pre-Notices to any federal agencies, including the NIH, even though the NIH is responsible for federally funded trials that have not reported mandated results to ClinicalTrials.gov. Instead, Pre-Notices were sent to industry, academia, and other organizations. NIH and FDA coordination is possible, as Pre-Notice templates have been cooperatively created.

2. Awareness at the FDA and NIH about Rampant Noncompliance

Senior FDA and NIH officials are aware of and concerned with clinical trial noncompliance, yet no substantive action has been taken. FOIA requests have shown that the FDA and NIH are aware of the power of Pre-Notice letters and Notices of Noncompliance. In emails between NIH officials, one NIH official expressed concern about the total percentages of trial results posted or submitted each year, which were substantially decreasing on a yearly basis (72% for 2018, 68% for 2019, 49% for 2020). Another NIH official wanted to “know what compliance rate the data represent” and cited concerns that they “may get questions from OSP” (the NIH Office of Science and Policy, responsible for analyzing NIH policy implementation as it pertains to the responsible conduct of research).⁵⁷ This evidence and the OIG findings demonstrate that NIH officials are aware of interagency pressure to improve responsible party compliance and data oversight of results reporting.

The FDA is also knowledgeable of underreporting and the efficacy of the agency's enforcement authority, even when applied minimally. The FDA knew that “in the few instances where FDA has issued a Notice of Noncompliance, the Notices have also been extremely effective.” Documents procured through UAEM's FOIA investigation show that the FDA and NIH are “proceeding towards enforcement action,” yet that action has been inconsistent, with only a small percentage of Pre-Notices issued. The FDA is aware of the power of Pre-Notice letters, given their high success rate in the past, and that they also preclude the need to levy fines or other penalties on responsible parties.

Problems

In response to compliance pressure, the NIH described how it enabled new internal quarterly reporting on trials that failed to meet their results submission deadlines on ClinicalTrials.gov. It is clear that the NIH is aware of noncompliance and is concerned with reporting deadlines. Now the onus is on the NIH and FDA to take broader, more significant action.

3. Lack of Enforcement Action

As has been discussed, Pre-Notices and Notices of Noncompliance are largely effective at increasing compliance. **The FDA has issued minimal Pre-Notices and Notices of Noncompliance despite the thousands of noncompliant responsible parties. However, the FDA has not made any commitments to increase the issuance of Notices.** As mentioned previously, the FDA produced a 2020 violation framework and guidance document to identify which noncompliant trials would receive Notices. However, the agency stated in the same document that the methodology would not “...operate to bind FDA” and that the agency would “generally intend to identify violations.”⁵⁸ The FDA’s statements show that the agency does not intend to apply consistent authority to regulate compliance in results reporting.

Furthermore, both the FDA and NIH can implement external catalysts after Pre-Notices to generate compliance. The FDA has the capability to impose civil money penalties, an additional powerful enforcement tool. As stated above, the FDA could have levied \$46 billion in fines as a result of FDAAA. In the April 2023 letter to U.S. Representative Frank Pallone, the FDA shared it has not imposed penalties given the Pre-Notice letters and Notices “are largely effective in securing compliance.” However, it is essential to maintain *consistent* compliance from sponsors.

4. External Catalysts to Enforcement

In 1992, the Prescription Drug User Fee Act (PDUFA) created a mechanism for drug manufacturers to pay “user fees” to the FDA for reviewing their prescription drug products for approval.⁵⁹ In 2002, the Medical Device User Fee and Modernization Act (MDUFMA) required medical device companies to pay the FDA for device approvals.⁶⁰ This legislation has been reauthorized every five years and has been followed by other user fee acts across biomedical approvals. In 2022, user fees represented 46% (\$2.9 billion) of the FDA’s total budget, which has allowed the FDA to hire additional staff to manage drug approvals.⁶¹ However, this funding also incentivizes the FDA to prioritize drug approval reviews, as is exemplified by the decrease in the FDA’s drug review times from more than 3 years in 1983 to less than 1 year in 2017; total time from the authorization of clinical testing to approval has remained at approximately 8 years over that period.⁶²

Problems

Other areas of the FDA's enforcement have been left underfunded and overlooked such as clinical trials oversight. In response to Congressman Dunn's letter, the FDA cited that the agency "considers which activities are likely to have the greatest public health impact and balances resource allocation to ClinicalTrials.gov with resource needs for other compliance programs...." This statement shows that the FDA does not prioritize resources towards strengthening compliance efforts and could increase funding requests to bolster regulatory efforts. **Yet, at the time of this writing, the Department of Health and Human Services Budget in Brief does not include a line item request for the Food and Drug Administration on clinical trial enforcement.**⁶³

Furthermore, the FDA's BIMO program has the responsibility of ensuring clinical trial data reporting, quality, and the welfare of human subjects.⁶⁴ In 2022, BIMO completed 900 domestic inspections and approximately 200 foreign inspections, yet the FDA reported only employing 89 BIMO inspectors.^{65,66} The FDA's budgetary authority for the 21st Century Cures Act is also insufficient for funding clinical trial oversight. In addition to the section 2052 reports on clinical trial enforcement, the 21st Century Cures Act requires the FDA to "accelerate development and review of certain medical products (e.g., combination products, antimicrobials, drugs for rare disease, and regenerative therapies)."⁶⁷ However, the appropriations allotted for the FDA to execute these tasks and 2052 reporting was only \$70 million in 2019 (1.2% of the FDA's FY 2019 budget), \$70 million in 2021 (1.1% of the FDA's FY 2021 budget), and \$50 million in FY2023 (0.60% of the FDA's FY 2023 budget).^{68,69,70} The FDA could request additional budget authority from Congress to better allocate resources to ClinicalTrials.gov oversight.

Policy Recommendations

First, and least burdensome, the FDA should send more Pre-Notices. The FDA has yet to send Pre-Notices or Notices of Noncompliance to thousands of responsible parties that have not reported results, including sponsors who are recipients of NIH grant money. The FDA could create an automated system to issue letters to every sponsor whose trials are potentially noncompliant after a certain date. The system does not need to require the agency to make a formal determination of noncompliance before issuing the letter, as it simply states that the party may be noncompliant.

Second, in Pre-Notices, the FDA should clarify enforcement procedures regarding action initiation timelines and potential monetary penalties. Currently, the FDA does not state in the Pre-Notice the subsequent enforcement actions that the FDA will take after a certain date. Although Pre-Notices are already very effective at generating compliance, UAEM found in its FOIA analysis that the FDA must often issue multiple Pre-Notices before sponsors take action.

Policy Recommendations

If the FDA were to include enforcement deadlines in the first Pre-Notice, sponsors would likely be more inclined to maintain reporting requirements. Further enforcement action could include levying civil money penalties.

Third, to help prioritize compliance under current budget constraints, the FDA should set and consistently apply objective criteria for prioritization of enforcement efforts. Utilizing an automated system to generate Pre-Notices would reduce the resources and time required by manual issuance. To this end, the agency could also request additional funding from Congress to sufficiently coordinate enforcement efforts with the NIH.

Fourth, the NIH should issue noncompliance letters for trials with NIH grant money, particularly outlining the potential withholding of grant money in accordance with the NIH's statutory authority. In this regard, the NIH should coordinate enforcement by updating the FDA with a list of noncompliant responsible parties.

Fifth, Congress should reauthorize Section 2052 reports from the 21st Century Cures Act to require reporting from the NIH and FDA on the status of compliance and enforcement with FDAAA every 2 years. These 2052 reports provide additional budget appropriations to further responsible party education and enforcement initiatives pursuant to FDAAA. Moreover, 2052 reports should be made publicly available to enable patient and physician access to the status of noncompliant clinical trials.

With these recommendations in place, clinical trial transparency can be improved in the United States and abroad.

If the FDA and NIH are able to better enforce FDAAA as written and close the gap on the 4,000+ clinical trials that lack reporting as of the writing of this report, patients and providers will have more reliable data to make informed health decisions.

Prioritization and a transparent, automated process for issuing Pre-Notices and Notices of Noncompliance will create greater accountability for responsible parties and encourage the sharing of clinical results that can help advance the field of medicine as a whole.

About UAEM

Universities Allied for Essential Medicines (UAEM) is an international health equity organization aimed at improving access to medicines and transparency in clinical research. UAEM operates largely via volunteerism on the part of students and academics in the fields of medicine, policy, and law. UAEM's Transparency Team has been working to promote timely results reporting to ClinicalTrials.gov since 2019.

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