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POSTER #29

Impact of Enforcement of FDA Amendments Act of 2007 on Clinical Trial Reporting Compliance

Tiha M. Long[a] and Dominic Fox[b]

[a]Envision Pharma Group, Connecticut, United States; [b]Envision Pharma Group, Wilmslow, United Kingdom

Background

- The US FDA Amendments Act of 2007 (FDAAA) is a law that came into effect for all clinical trials due after **January 18, 2017**, which requires clinical trial sponsors to submit results to clinicaltrials.gov within one year of the study's completion[1]
- In **August 2020,** the FDA established guidance for civil money penalties relating to FDAAA noncompliance[2]
- Prior to April 2021, the FDA issued approximately 40 Pre-Notices of Noncompliance to encourage voluntary compliance[3]
- In **April 2021,** the FDA issued the first Notice of Noncompliance with a threat of financial penalty[4]
- Additional Notices of Noncompliance were issued by the FDA in August 2021 and April 2022[5]

Objective

- Our goal was to determine if the actions taken by the FDA to issue clinical trial sponsors with Notices of Noncompliance have impacted compliance with the FDAAA regulation

Significance

- The reporting of clinical trial results supports access to information to bolster informed decision making by healthcare providers for the treatment of patients
  - Despite the importance of access to trial results, only 76% of clinical trials results have been reported (February 2018 – March 2023)
- The FDAAA 2007 law requires that sponsors report clinical trial results under the threat of financial penalty
  - As of March 2023, the US government could have imposed fines totalling more than $45 billion to clinical trial sponsors
- The FDA has indeed issued several Notices of Noncompliance to FDAAA 2007 to non-reporting clinical trial sponsors with threats of financial penalties
  - Recent actions by the FDA may indicate a shift toward increased enforcement of FDAAA 2007[6]

Results

- Approximately 42% of trials due to report were sponsored by industry. Most trials due to report were Phase 2 (~31%) and Phase 3 clinical trials (~16%). The majority of trials were located in the US (~69%) or in the US and another country (~19%) **(Table 1)**
- On October 14, 2022, the ClinicalTrials.gov database contained a total of 430,639 trials
- After excluding trials that were neither an applicable clinical trial (ACT) nor a probable ACT under the Final Rule, those that were not yet due to report results, and trials that had received a certificate of delay from ClinicalTrials.gov, there were 13,914 trials identified as due to report results by September 2022 under the Final Rule of FDAAA
- Annual trends for compliance with FDAAA fluctuated slightly from 38.0% in 2018, to the highest level of 40.9% in 2021, and down to 37.5% in 2022 **(Figure 1)**
  - Following the onset of COVID-19 in March 2020, the data show a trend of decreasing compliance to July 2020, of 40.8% to 39.5%, followed by a recovery in compliance in November 2020, reaching 40.9% **(Figure 1)**
- We observed a small but significant (p<0.001) increase in compliance after April 2021 (42.3%) compared to before April 2021 (40.7%) **(Figure 1)**
- Overall, the median delay from primary completion date to submission date was 480 days (95% CI 475–489), 115 days longer than the legal reporting requirement of 1 year **(Figure 2)**
  - Industry sponsors aggressively increase their trial reporting as they approach their due date as compared to non-industry sponsors
- After May 2021, when the FDA announced the first Notice of Noncompliance, the median delay to submission was 436 days (95% CI 428–442) **(Figure 2)**
- For noncompliant, overdue trials, an industry-sponsored trial is more likely to remain unreported than a non-industry sponsored trial **(Figure 3)**

Tables and figures

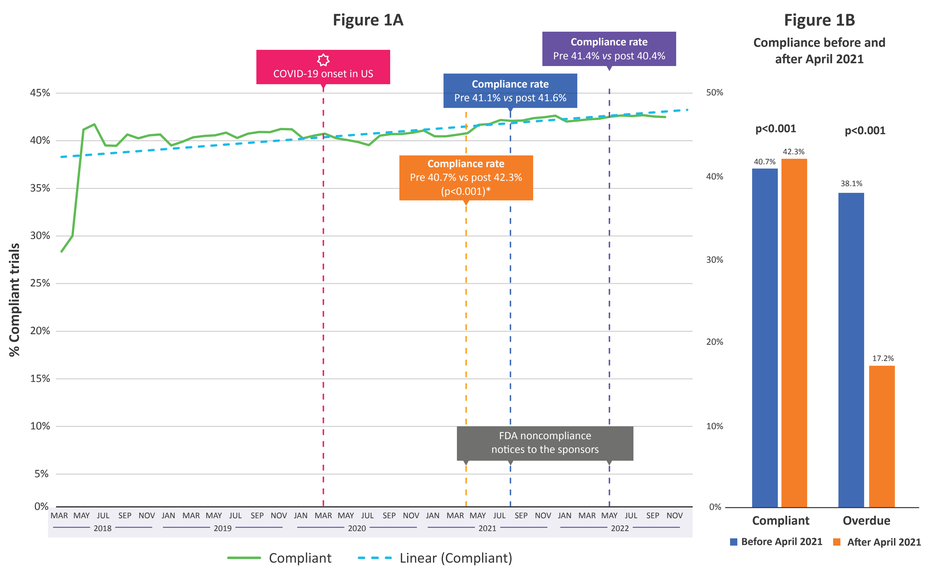
Table 1. Reported and compliant applicable clinical trials from January 2018 through September 2022

	Trials due to report (n=13,914)	Trials with any results (10,226 [73.5%])	Compliant trials (5774 [56.5%])
Sponsor type			
Industry	5889 (42.32%)	4320 (42.25%)	2905 (50.31%)
National Institutes of Health	405 (2.91%)	393 (3.84%)	182 (3.15%)
Non-industry*	7441 (53.48%)	5420 (53%)	2650 (45.9%)
US government	179 (1.29%)	93 (0.91%)	37 (0.64%)
Phase			
Not available	3820 (27.45%)	2408 (23.55%)	1147 (19.86%)
Phase 1/Phase 2	1166 (8.38%)	862 (8.43%)	485 (8.4%)
Phase 2	4360 (31.34%)	3517 (34.39%)	1986 (34.4%)
Phase 2/Phase 3	367 (2.64%)	248 (2.43%)	132 (2.29%)
Phase 3	2238 (16.08%)	1847 (18.06%)	1286 (22.27%)
Phase 4	1963 (14.11%)	1344 (13.14%)	738 (12.78%)
Trial location			
No US location	1304 (9.37%)	599 (5.86%)	373 (6.46%)
No location data available	295 (2.12%)	93 (0.91%)	55 (0.95%)
US and other country	2697 (19.38%)	2376 (23.23%)	1758 (30.45%)
US only	9618 (69.13%)	7158 (70%)	3588 (62.14%)

**Individuals, universities, or community-based organizations*

Figure 1. Trends in compliance rates

Compliance rates were compared before and after noncompliance notices were issued by the FDA to clinical trial sponsors (Figure 1A); compliance before and after April 2021 (Figure 1B).



Tables and figures

Figure 2. Kaplan-Meier curve showing time to reporting from primary completion date for trials by industry and non-industry sponsors

Figure 2 shows cumulative time to reporting for trials from January 2018 through September 2022. The dashed vertical line indicates the 1-year deadline by which trials should report their results according to FDAAA 2007. Compared with non-industry sponsors, industry sponsors increase their trial reporting as they approach their due date.

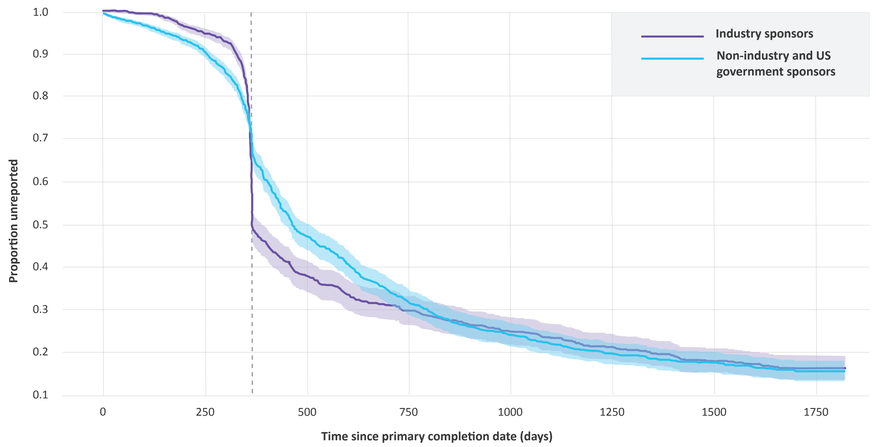
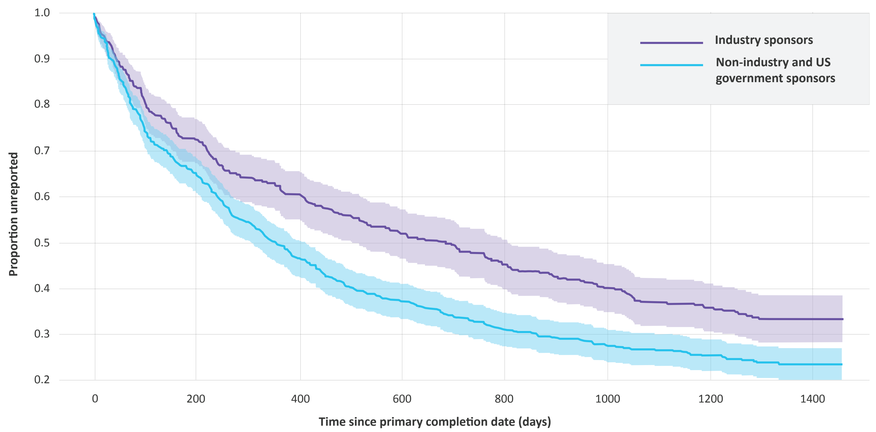


Figure 3. Kaplan-Meier curves showing days late for overdue trials by industry and non-industry sponsors

Figure 3 shows cumulative days late for overdue noncompliant trials that did not have results reported 1 year after their primary completion date, from January 2018 through September 2022.



Conclusions

- Compliance with the FDAAA regulation remains poor
- The small but significant increase in compliance after April 2021 may be related to issuance of the first Notice of Noncompliance with threat of financial penalty
- This finding suggests that actions by regulators may improve compliance

References

1.FDAAA 801 and the Final Rule. https://clinicaltrials.gov/ct2/manage-recs/fdaaa. Acccessed April 12, 2023. 2. OGCP, CDER, CBER, CDRH, ORA. Civil Money Penalties Relating to the ClinicalTrials.gov Data Bank. https://www.fda.gov/media/113361/download. Published August 2020. Accessed March 20, 2023. 3. Woodcock J. FDA takes action for failure to submit required clinical trial results information to clinicaltrials.gov. Press Announcements: FDA Statement. https://www.fda.gov/news-events/press-announcements/fda-takes-action-failure-submit-required-clinical-trial-results-information-clinicaltrialsgov. Published April 28, 2021. Accessed March 20, 2023. 4. McMeekin J. Notice of noncompliance issued pursuant to 42 U.S.C. 282(j)(5)(C)(ii). U.S. Food & Drug Administration. https://www.fda.gov/media/148036/download. Published April 27, 2021. Accessed January 11, 2023. 5. U.S. Food & Drug Administration. Notices of Noncompliance and Civil Money Penalty Actions. https://www.fda.gov/science-research/fdas-role-clinicaltrialsgov-information/clinicaltrialsgov-notices-noncompliance-and-civil-money-penalty-actions. Accessed April 12, 2023. 6. Medscape. FDA Signals Tougher Stance on Required ClinicalTrials.Gov Postings. https://www.medscape.com/viewarticle/951508. Published November 6, 2021. Accessed March 20, 2023.

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Keywords

Compliance, Food and Drug Administration (FDA), and Legal/Regulatory

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