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Compliance with Clinical Trials Reporting Requirements of the FDA Amendments Act 2007

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Introduction

The FDA Amendments Act of 2007 (FDAAA 2007) and its associated 2016 Final Rule require most interventional clinical trials in drugs, devices, and biologics regulated by the US Food and Drug Administration to reports results directly to ClinicalTrials.gov within 1 year of primary completion.[1 2 3] The Final Rule details which trials are required to report and how they should report. This poster details compliance with the reporting requirements of the FDAAA 2007, as outlined in the Final Rule, along with quantitative assessments of various related requirements. This data is preliminary and being prepared, along with additional findings, for future publication.

Methods

The FDAAA 2007 and its associated Final Rule were reviewed for requirements that could be assessed quantitatively with data directly from ClinicalTrials.gov. As part of the TrialsTracker project (fdaaa.trialstracker.net), a full version of ClinicalTrials.gov is archived every working day and processed to assess the results status of all covered trials under the FDAAA 2007. Adapting the methods developed for the FDAAA TrialsTracker[4] we identified applicable trials and extracted relevant study details from ClinicalTrials.gov for each analysis. All data handling and processing was performed in Python 3.7.

Results

Reporting Trends

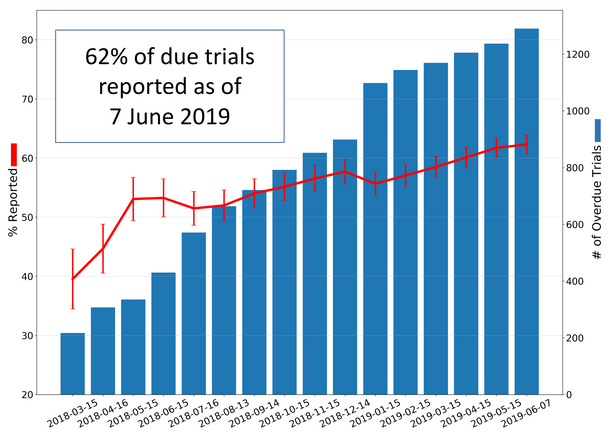

Figure 1. Reporting Percentage and Overdue Trials By Month.

- Sponsors of applicable trials must report results "no later than 1 year after the primary completion date of the applicable clinical trial"

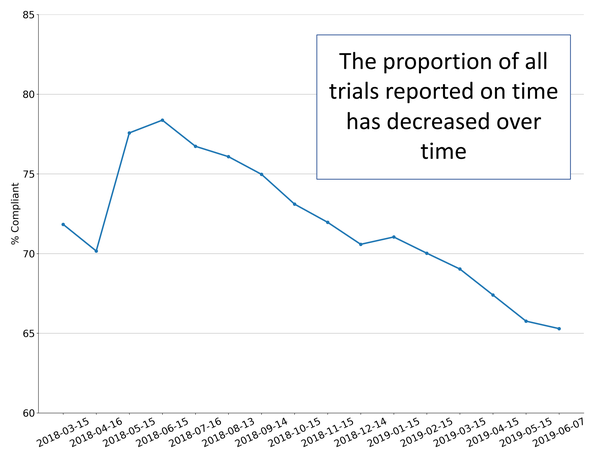

Figure 2. Percent of Results Reported Within One Year of Primary Completion

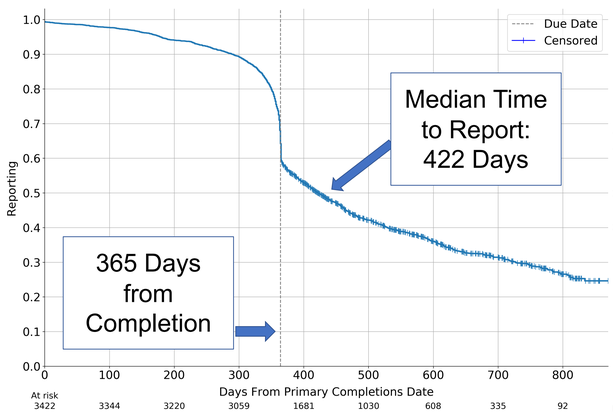

Figure 3. Time To Reporting From Primary Completion

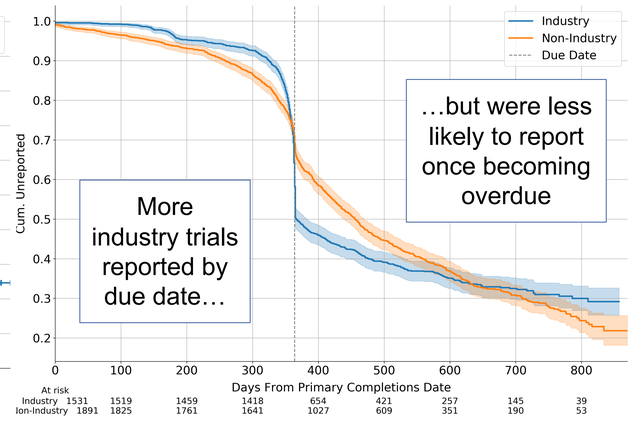

Figure 4. Time To Reporting From Primary Completion – Industry & Non-Industry Sponsors

Quality Control (QC)

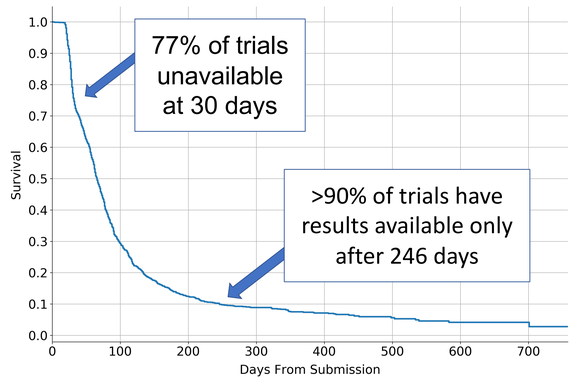

Figure 5. Time To Results Availability From Submission

- The Final Rule requires ClincialTrials.gov to post results within 30 days regardless of QC status.
- If submitted results fail QC, sponsors must resubmit results within 25 days.
  - 54% of 2466 trials had results returned at least once;
  - 25% of resubmissions were late (18% of trials);
  - The mean time to resubmission was 28 days with a max of 462 days

Document Availability

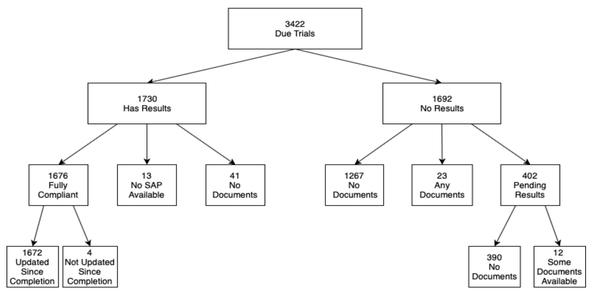

Figure 6. Status of Trial Documentation for Due Trials

- Sponsors must submit a protocol and statistical analysis plan (SAP) with results.
  - 1730 due trials were assessed;
  - 1676 (97%) contained all required documentation;
  - 13 (<1%) stated no SAP existed and 41 (2%) had results but lacked any documentation.

Certificates of Delay

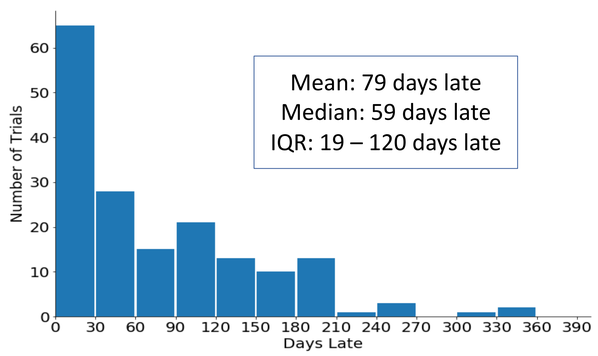

Figure 7. Days Late to Apply for Certificate of Delay

- Sponsors must apply for a certificate to delay results reporting but this should occur before results are otherwise due
  - 29% of 597 documented certificates were submitted late.

Ideas to improve reporting?

Experiences to share?

Feedback?

Get in touch!

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Reporting Secondary Outcomes – Pilot Data

Reported Fully	Reported With Potential Issues	Unreported
10	8	2

Table 1. Secondary Outcome Reporting Status

- Sponsors must update results to include full secondary outcome and safety data within a year of full study completion. Pilot data was collected to determine how compliance with this requirement could by systematically assessed.
  - 20 trials were identified that had full completion dates after their primary completion date and first submitted results prior to full completion;
  - For each trial, the ClinicalTrials.gov study record, results, and update history were assessed for the completeness of reporting
- Of the 20 trials:
  - 10 had fully reported all outcomes;
  - 2 had confirmed unreported secondary outcomes;
  - 8 reported all outcomes but either have not updated their record post full-completion (1) or have outcome timeframes that do not match the dates provided (7)
- Data issues may complicate the automated assessment of secondary outcome reporting and a more complex and resource intensive methodology that manually considers the protocol, study design, and details of outcomes is likely required.

Conclusions & Discussion

Conclusions:

- As of 7 June 2019, 38% of applicable trials required to report have submitted no results; of due trials that did report, 35% reported late. Median time to report (422 days) is greater than the required reporting deadline (365 days).
- While the availability of documentation was high among reported trials, other areas raise concerns about the trial reporting process. The QC and Certificate of Delay procedures are both operating outside of the guidelines established in the Final Rule.
- Pilot data on secondary outcome reporting indicate future research on the extent of compliance with the requirement is warranted but would require additional resource and methods development to ensure accurate assessments.

Discussion:

Compliance with the reporting requirements of the FDAAA 2007 and its Final Rule is uneven and represents a failure to fully implement the law as described. Issues with the implementation and enforcement of the law continue to undermine the complete and prompt sharing of results more than 2 years after the Final Rule came into effect. Ignoring these clearly established requirements delays the availability of results and reinforces lax reporting behavior by sponsors.

In our experience with the FDAAA TrialsTracker these unreported trials represent a combination of genuinely overdue trials and trials with incorrect or out-of-date information on the Tracker, both of which are violations of the FDAAA 2007. To date we know of no fines, nor other enforcement actions, that have been taken by the FDA pursuant to non-compliance with the reporting requirements of the FDAAA 2007.

Effective implementation and enforcement of the FDAAA 2007 is necessary to ensure the legislative goals of complete, accurate, and timely reporting of clinical trials are realized.

FDAAA TrialsTracker

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Data Sharing & Code

Github | FDAAA TT | Get in Touch

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1. Dept. of Health and Human Services. Final Rule - Clinical Trials Registration and Results Information Submission. 2016;**81**:64982–5157.
2. Food and Drug Administration Amendments Act of 2007.
3. Zarin DA, Tse T, Williams RJ, *et al.* Trial Reporting in ClinicalTrials.gov - The Final Rule. *N Engl J Med* 2016;**375**:1998–2004.
4. DeVito NJ, Bacon S, Goldacre B. FDAAA TrialsTracker: A live informatics tool to monitor compliance with FDA requirements to report clinical trial results. bioRxiv. 2018;:266452. doi:10.1101/266452

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