Clinical Trial Identifiers in Publications and Accessibility of Clinical Trial Data

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Abstract
Background and Objective: The GPP and ICMJE guidelines and FDAAA regulations mandated increased transparency of clinical trial results from pharmaceutical company-sponsored trials. This study examined compliance with these guidelines as well as accessibility of trial results and publications.

Methods: Peer-reviewed publications reporting clinical trial results for 3 chronic obstructive pulmonary disease (COPD) clinical trials manufactured by 3 different pharmaceutical companies (published 2004-2009) were examined for inclusion of clinical trial identifiers (ACT, NCT number, company trial number). Accessibility of trial results and publications from ClinicalTrials.gov were also checked. Results: The number of pharmaceutical company-sponsored publications containing any trial identifier in the PubMed abstract rose from 4/12 (33%) to 13/22 (59%) over the last 4 years. No publications reported the NCT number in the abstract or text in 2004-05, but all 2009 publications did. Using NCT numbers as a search term on PubMed retrieved only 24 of the 83 corresponding publications, and these 24 publications were accessible through links from ClinicalTrials.gov listings. Few (8%) trials directly posted results on ClinicalTrials.gov, but most (86%) trial results were available on company websites, although not identified by NCT number. Of the 8 trials required by FDAAA regulations to post results, 7 trials listed on ClinicalTrials.gov and/or company websites. Conclusions: Although it can be difficult to match clinical trial identifiers to publications, increased and accessible access is improving, possibly because of increased compliance and new regulations.

Objective
This analysis examined the accessibility of clinical trial data and publications reporting primary or secondary analyses of these 3 companies. In addition, a different therapeutic area may also yield different results.

Background
Timeline of guidelines and regulations relevant to clinical trials and reporting of results:

- Although the Food and Drug Administration Modernization Act (FDAMA) required trial registration, there was no enforcement strategy.
- The Food and Drug Administration Amendments Act (FDAAA) is the first FDA regulation to require clinical trial registration and posting of results, and this law went into effect on 9/27/07. All trials that began on or after this date must be registered.
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- The FDAAA-mandated timing of trial registration and posting of results

Methods
Search strategy:

- PubMed search
- ClinicalTrials.gov search
- Company websites

Results
Inclusion of any trial identifiers in PubMed abstracts

Publication retrieved from a search of PubMed with a trial’s NCT number

Number of trials

Trials ending in 2008 or earlier:

- 88% have results posted on the company website and/or ClinicalTrials.gov.
- 97% of the clinical trial publications from company A list a trial identifier in the abstract or text.
- 75% from company C.

Company variation in listing any trial identifier anywhere in a publication

Figure 5. Percentage of PubMed abstracts of all 3 drugs included the NCT number, company clinical trial number, or study name in the abstract or text. Note that all articles can have ≥1 trial identifier.

- No trial identifiers appear in the abstract for the rest of the trials.
- Near all (95%) of the 2009 publications included a trial identifier somewhere in the paper.
- Inclusion of the company study number appears to be decreasing, whereas usage of the NCT number is increasing.

Figure 6. Distribution of PubMed abstracts with any trial identifier.

- Of the 83 publications to which we were able to match an NCT number, 24 (30%) of them were retrieved from a PubMed search using the NCT number or the search term "ClinicalTrials.gov"
- Retrievability of the sponsored publications varied widely among the 3 companies, 59% of the published trials retrieved from company A were retrieved within 16% of those from company B and 100% from company C.

Figure 7. Inclusion of any trial identifier anywhere in the paper.

- 97% of the clinical trial publications from company A list a trial identifier in the abstract or text.
- 75% from company C.
- No trial identifiers appear in the abstract for the rest of the trials.
- Near all (95%) of the 2009 publications included a trial identifier somewhere in the paper.
- Inclusion of the company study number appears to be decreasing, whereas usage of the NCT number is increasing.

Figure 8. Inclusion of any trial identifier anywhere in the paper.

Limitations of this analysis
This study examined only clinical trials of 3 drugs indicated for COPD. It is possible that different results would be obtained using clinical trials sponsored by different pharmaceutical companies, especially since there is wide variation in clinical trial identifiers reporting in publications and posting of clinical trial results among these 3 companies. In addition, a different therapeutic area may also yield different results.

Discussion
- Clinical accessibility and cross-referencing of clinical trial results and publications has increased since FDAAA took effect.
- Inclusion of a trial identifier in the abstract of a publication is important for visibility and ease of cross-referencing to a given trial. There were a few cases in which a trial identifier was available in the abstract on the journal’s website, but not in the PubMed abstract. Thus, journal editors should aim to include trial identification numbers in PubMed search terms.
- Clinical trial registries need to be kept up to date. Despite the yearly update requirement for ClinicalTrials.gov, several listings did not include start and/or end dates, and others were completed but were still listed as ongoing.
- Future work will focus on trial registration and reporting of clinical trials that are not industry-sponsored.

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Figure 10. The number of PubMed abstracts (%)

- 20
- 30
- 40
- 50
- 60
- 70
- 80
- 90
- 100

Figure 14. The NCT number was used as a search term to retrieve publications of trial results.

- Of the 83 publications to which we were able to match an NCT number, 24 (30%) of them were retrieved from a PubMed search using the NCT number or the search term "ClinicalTrials.gov"
- Retrievability of the sponsored publications varied widely among the 3 companies. 59% of the published trials retrieved from company A were retrieved within 16% of those from company B and 100% from company C.
- Retrieved publications were also all listed on ClinicalTrials.gov for each corresponding trial.

Figures 11 & 12. Inclusion of any trial identifier anywhere in the paper.

- 97% of the clinical trial publications from company A list a trial identifier in the abstract or text.
- 75% from company C.
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- Near all (95%) of the 2009 publications included a trial identifier somewhere in the paper.
- Inclusion of the company study number appears to be decreasing, whereas usage of the NCT number is increasing.

Figure 13. Posts ending in 2008 were not included in this graph since trial sponsor can post results within 1 year of the trial end date.

- Of the trials ending in 2008 or earlier, 88% have results posted on the company’s website. Note that these 3 companies list their clinical trials by company trial number, not NCT number.
- Only 6% of the completed trials posted their results on ClinicalTrials.gov.
- Based on the company websites shown, all trials in this analysis should adhere to the FDAAA regulations. Of these, 7 have results posted on company web sites and/or ClinicalTrials.gov.

Figure 15. Inclusion of any trial identifier anywhere in the paper.

- 97% of the clinical trial publications from company A list a trial identifier in the abstract or text.
- 75% from company C.
- No trial identifiers appear in the abstract for the rest of the trials.
- Near all (95%) of the 2009 publications included a trial identifier somewhere in the paper.
- Inclusion of the company study number appears to be decreasing, whereas usage of the NCT number is increasing.

Figure 16. Distribution of PubMed abstracts with any trial identifier.