Reviewer's report

Title: Do Trialists Endorse Clinical Trial Registration? Survey of a PUBMED Sample.

Version: 2 Date: 10 May 2007

Reviewer: Erick Turner

Reviewer's report:

General
incorporated into comments below

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The authors should acknowledge “competing” initiatives that speak to the same issues. These are summarized in the Institute of Medicine report—which should be cited—and includes the ICJME mandate to register clinical trials as a condition for publication, the pharmaceutical industry’s commitment to register clinical trials results and to post their results.

It would be very helpful to see the actual survey. How questions are worded can shape their responses. (For example, “Would you agree that all clinical trials results should be made available so that the public health can benefit?” versus “Would you agree that not all trials need to be reported on, such as trials that are grossly underpowered or with fatal methodological flaws?” You would get very different responses to these two questions.) Could the survey be made accessible as part of the manuscript through a hyperlink though not necessarily part of the body of the paper?

Results, first paragraph: You point out that the response rate was particularly low in the US, but the only thing the reader has to compare that with is the 60% figure for all 45 countries taken together. Please mention response rates in the other countries with the largest number of responders. Warning: adding these numbers to those in the preceding sentence will make it more confusing to read if it is left in prose format. As per other comments, consider putting this information in table format if editorial policy permits.

Why are devices, but not drugs, mentioned at the top of page 9?

Reference number 15 is used for a point about Phase 1 trials and the US Federal [sic, see below] Drug Administration. I checked the cited document and found no mention of the FDA or Phase 1 trials or of devices. I don’t understand why Phase 1 trials are mentioned here because they do not involve testing of the drug for efficacy. The FDA reviews focus more on Phase 2 and Phase 3 trials. True, these reviews are available only if the drugs are approved by the FDA for the indication in question. If you need a reference for this, there is an essay I wrote in PLoS Medicine 2004, available at http://dx.doi.org/10.1371/journal.pmed.0010060. However, you are welcome to try to find another reference.

Page 10, second paragraph: Did you have a question at the beginning assessing their prior knowledge or familiarity with this? For those researchers that were relatively naïve to this topic—you correctly say on page 4 that there is a lack of awareness among researchers regarding the importance of the problem—it could be argued that the act of completing the survey was a learning experience for them and that you were shaping their attitudes on this topic. Thus, it seems possible that naïve respondents might respond differently from respondents who are well aware of the problem (not to suggest that people with an awareness are monolithic in their attitudes toward registration).

The last sentence of the Discussion largely duplicates the second sentence in the Discussion. You say the discrepancy between the 64% and the 47% figures is “interesting”, but why? Are you suggesting they are hypocritical? If so, you can’t say that in so many words. But nor can you just coyly dangle the “interesting” without any elaboration. See related discretionary comment below.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
When discussing studies to follow up on this study, it seems a valuable approach would be to use the tools of so-called descriptive research. The authors did receive input from a few respondents as to their objections to full registration. A descriptive approach—as opposed to the quantitative approach employed here—would allow this to be fleshed out. If the areas of disagreement between proponents and opponents of registration can be clarified, then we will further along toward reaching a consensus (instead of it being a more adversarial process).

Can some of the results be presented in a more reader-friendly form, such as in tables? It’s difficult and somewhat dry reading in prose format.

FDA stands for “Food and Drug Administration”.

For the “intelligence companies” listed in parentheses, I think you mean to use the abbreviation e.g. (“for example”), not i.e. (“that is,”), which would suggest that those are the only two such companies.

The point about “A universal requirement for clinical trial registration as a condition of ethics approval…” should be referenced, since the suggestion is not original to this article. A quick search turned up this editorial by Fiona Godlee in the BMJ: BMJ 2006;332:1107-1108 (13 May), doi:10.1136/bmj.332.7550.1107. It is possible that that suggestion might have been made even earlier. Please check this out and cite the original reference.

On page 10, regarding the limitations to PubMed, I seem to recall learning from reference librarians that PubMed is biased toward English-language journals and that is has poorer coverage of European journals than, say, Biosis (and others)? I believe this is the reason why systematic literature reviews, such as Cochrane reviews, go beyond PubMed. If this is true, this should be mentioned as a limitation.

Last sentence in Discussion, “researcher’s difficulties to handle sponsor’s interests”. There are a few grammatical problems here that could be left to the copy editor, if the paper is accepted, but this can probably be reworded by a co-author who is a native speaker of English.

Duplication of references: #4 and #11 refer to the same work.

In Table 1, please highlight the items the 5 protocol items felt by industry to be commercially sensitive, which are discussed beginning at the bottom of page 4. These 5 “bones of contention” should be emphasized in order to bring more pressure to bear upon those who are arguing to keep them secret.

Boxes 1, 2, 3: These should be put in the form of tables, ie. with the numbers falling under one another in columns. This would make the boxes more reader-friendly.

Boxes 1,2, 3: Question for editors: Should these numbers be represented in graphical format to help the reader grasp the relative proportions, or is this discouraged in Trials?

Discretionary Revisions (which the author can choose to ignore)

The point that the information is not really secret because “intelligence companies” apparently have access to it is a good one. It raises the question, How do they get it, then? Is there an überclass that is getting this valuable information while the people that really should be getting it are denied access? To deal with in any detail would be beyond the scope of this paper, but it might be worth a sentence in the discussion if you can find an answer.

I agree with the point about subjectivity in the use of the word “key” as applied to secondary endpoints. It may be of interest to see whether there is an agreed-upon definition of “key”. On the other hand, if the decision is arbitrary, could this be a way for a pharmaceutical company to keep more information secret than is warranted?

Last sentence of Discussion involving the “interesting” discrepancy between 64% and 47%. (related to comment under Major Revisions). This reminds me of the JAMA paper that reported that doctors, when surveyed, say that many of their colleagues are conflicted with drug company ties, but at the same time they say that they personally are not conflicted. You might consider consulting with someone with knowledge of cognitive psychology to see what this phenomenon is known as.)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.