Reviewer's report

Title: Clinical drug trials in general practice: a ten-year overview of protocols

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Reviewer: Louise Berendt

Reviewer's report:

Summary
The study aims to describe selected characteristics of clinical drug trials in general practice in Norway. Methodologically the study was conducted as a cohort study of clinical drug trial applications submitted to the Norwegian Medicines Agency in the period 1998-2007. Previous studies have reported characteristics of Norwegian clinical drug trials, but not for general practice trials in particular. The major findings were that only a fraction of Norwegian clinical drug trials are conducted in general practice, of which very few are non-commercial trials.

In general, the research question is relevant and the manuscript well written.

Major compulsory revisions
1. The time of collecting the data should be stated, including the time of conduct of the literature search related to the ONE trial. It should also be stated whether all of the included applications were approved by the Norwegian Medicines Agency or if any were rejected.

2. A few files may easily be missing from a large archive of historical trials. However, no reasons for exclusion are given in the flow chart when selecting 196 of the 2,054 trials. Does this mean that all applications received by the Norwegian Medicines Agency in the period were available as a paper file in the archive?

3. Methods for minimising errors during data collection should be described. Is it correct that data collection was conducted by a single assessor?

Discretionary revisions
3. Background, fifth and sixth paragraph: It is mentioned that previous studies have demonstrated a low output of scientifically valid and clinically relevant results and a low rate of randomised controlled trials in general practice. It would be interesting to know whether this also holds for clinical drug trials in Norwegian general practice.

4. Methods, sixth paragraph: Various methods of classifying trials as industry-initiated/industry-funded/commercial and researcher-initiated/non-commercial/academic exist. In this study, the categorisation was based on the source of funding, who wrote the study protocol,
and who conducted the study. It is stated that trials funded by a pharmaceutical company was categorised as industry-initiated. Does this categorisation take into account the situation of a clinical trial partially funded by a pharmaceutical company (e.g. by receiving the study drugs free of charge), but otherwise designed and conducted under the responsibility of a GP? Furthermore, it is not clear to me how trials with unclear funding were handled (e.g. an application stating that further external funding will be applied for). This should be specified.

5. In the time period 1998-2007, the European Clinical Trials Directive 2001/20/EC were enforced. With the directive came a formal definition of investigator-initiated clinical drug trials. In your opinion, would a classification of the trials in your sample according to the definition in the directive lead to different results?

6. Discussion, second paragraph: Three studies assessing the proportion of non-commercial clinical drug trials are cited. Similar results from Danish clinical drug trials is available: Berendt et al, BMJ 2008;336:33-35.

7. The term ‘GP academics’ should be clarified.

8. It is unclear to me whether the terms “non-industry”, “non-commercial”, and “researcher-initiated” are used synonymously. Are they all to be thought of as antonyms of “industry-initiated trials” as defined in Methods, paragraph 6? If so, I would recommend the use of these terms to be streamlined as much as possible.

Minor issues not for publication

9. Punctuation is missing in Methods, paragraph 8.

10. Two tables are named “Table 3” and there is no “Table 2”.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests.

Although I have experience with the methodology used, I am not familiar with trials in general practice in particular. Therefore, my comments are concerned primarily with the methodological aspects of the study and the field of clinical drug trials in general.