Reviewer’s report

Title: Risk proportionate clinical trial monitoring: an example approach from a non-commercial trials unit

Version: 2 Date: 24 June 2013

Reviewer: Oana Brosteanu

Reviewer’s report:

- Major Compulsory Revisions

This is an interesting manuscript for those working in the field of non-commercial clinical trials. Since a few years, we experience a paradigm shift with respect to quality management of clinical trials, in favour of a risk-based approach tailored to the needs of the respective trial.

However, most of the published recommendations remain on a general level and do not provide specific details how to implement risk proportionate approaches. Therefore, we are in need for practical examples, and I encourage the publication of this manuscript.

However, in my opinion the following revisions should be incorporated:

1. The authors mention the risk-assessment they perform for each trial (page 6), and provide an example as a supplement. A description of the risk-assessment procedure is missing in the manuscript and should be added. At least the following aspects should be covered:
   a. Who is involved in risk-assessment?
   b. How are the risk categories identified?
   c. What are the provisions if a trial has overall a low risk, but there is one or more risk category with a high (>10) or even very high (>=20) score? Why on the first page of the risk-assessment only the mean score is mentioned and not the maximum score?

2. In Section 3 (page 7) the authors briefly mention the monitoring plan they develop based on prior risk-assessment, and provide an example as a further supplement. Here again, a more detailed description on the contents of the monitoring plan would be helpful for the readers, since the example provided is not in all parts self-explaining.

3. In section 3.2.1.1. (page 9) the authors mention that in general copies of completed informed consent forms are faxed to the CTRC. The authors should comment on data protection issues pertinent to this procedure. Are full names faxed?

- Minor Essential Revisions
4. The sentence “The purpose of this paper…” (Abstract - Purpose) should be rephrased. It remains unclear to what “relevant to standard clinical practice” refers.

5. In Figure 4, in all three diagrams the scale for the y-axis is missing.

6. The authors remark that the “trial monitoring report should not be confused with the reports … [for] the IDSMC”. A brief description of the contents of the IDSMC report should be added for less experienced readers.

- Discretionary Revisions

7. In Figure 1, I would prefer a flow diagram (with a loop) to the circle depicted.

8. An example for a monitoring report would be helpful.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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