**Manuscript evaluation guidelines**

**Title:** **Addressing Human Subjects Protections in Developing Countries**

**Date:** **11/04/18**

**Reviewer: R Ravinetto**

**CoI:** I personally know Francis Crawley and we had some collaboration in the past.

**1. Importance of the paper: does it address issues relevant to the fields of bioethics and medical ethics in the developing countries?**

In principle, yes. But when it comes to the full manuscript, it does not have a clear focus/scope. Details of observed weaknesses are listed below, in the separate comments for authors.

**2. Is it topical? Is the issue discussed from another country's/culture perspective?**

As said below (in the separate comments for authors), even if the title refers to “developing countries”, in practice it is not clear how developing countries are defined, e.g. is the focus on LMICs, or on LICs, or other? Or maybe on the Asian region, since at a certain time point the focus shifts on FERCAP/SIDCER?

**Will it influence practice or policy?** I do not think so, due to lack of focus, but also and mainly because lack of originality (more details below, in the separate comments for authors).

**Is it too specialized for the journal?** No, but I would say that it is too vague and generic.

3. **Originality. Is the information /comment new?** No. **Is there any likelihood of plagiarism?** No

**4. Conclusions:** quite surprisingly, there is not a formal Conclusion.

**5. Other comments**: NA

**6. Recommendation**: I would either refuse, or ask to submit a completely new paper (I am afraid I would surely not accept it at this stage).

**7. Separate comments for the author**

- The title is too broad and does not reflect the focus of the paper on three specific issues.

- If the main objective of the paper is presenting the FERCAP/SIDCER approach, this should be explicit in the title and abstract.

- The scope of the paper is not clearly defined, and not consistently defined through the text. Is it about clinical trials, clinical research, medical research or research in a broader sense?

- Even if the title refers to “developing countries”, in practice it is not clear how developing countries are defined, e.g. is the focus on LMICs, or on LICs, or other? Or maybe on the Asian region, since at a certain time point the focus shifts on FERCAP/SIDCER?

- Linked to the above, the sentence “the scientific culture of developed countries has proceeded at a different rate with more advanced structures than that in less developed countries (5)” is problematic: if it refers to LMICs as a whole, you can hardy attribute a same “rate” to all of them; in addition, it should be supported by more references (the only reference seems to be specific to the context of Turkey). The same may apply to other sentences, such as “Many ethical committees in developing countries were formed only recently and are still not sufficiently trained or equipped to function effectively when addressing challenging research protocols in difficult environments”; “The regulations regarding human subject protections in developing countries are also often lacking and underdeveloped”; “Furthermore, sensitive cultural differences can also impede the full implementation of what is generally considered best practices”.

- On a related note, it is not always clear if/to what extent the recommendations/reflections in this paper are specific to DCs. For instance, the fact that “the lengthy ICFs decrease the ability of potential research participants to comprehend the ICF content (11)”, or that “by clearly stating whether ethical approval and inform consent was obtain, how and from where they were obtained, or reasons why they were not obtained, peer-reviewers and journal editors can clearly assess whether the research was conducted ethically prior to giving their approval”, are equally relevant in affluent countries.

- Many sentences through the text should be supported by more up-to-date literature

- The main focus of the paper is on informed consent and ethics review. There is general consensus that these are essential for protection of human subjects, and there is also a vast literature on them; the paper does not seem to provide original reflection, nor new or innovative approaches to them. Corollary to this, the paper ignores new and less understood challenges to protection of participants in LMICs, linked for instance to community engagement, benefit sharing, data sharing, bio-banking and ownership of samples, inclusion of pregnant women in trials, research conducted in the frame of public health emergencies, etc.

- When it comes to the SICDER recognition program for ethics committees, some practical information would have been helpful to better understand its added value compared to other initiatives. For instance, are the detailed “Standards” open access (as a reviewer, I find it difficult to assess the paper without seeing them)? Who are the evaluators? Is the evaluation funded by SIDCER or by the evaluated ECs? Are there reevaluations over time? etc. It should also be explained more clearly if this a formal accreditation, if there are mutual recognition systems already in place across countries with SIDCER-approved ECs, and which organizations/countries formally endorse the recognition program (the sentence on Thailand and Philippines is not sufficient to understand this). When talking of “the international experiences of the SIDCER surveyors, particularly on the review of multi-countries clinical trials of new investigational products which are increasing in number in Asian countries”, describing a couple of concrete examples would have been helpful.

- On a related note, the SIDCER standards for recognition seem, based on the information available in Table I, to be mainly on “procedural aspects” rather than on “contents aspects”. A more detailed description of the contents/methodology of the evaluation, would have helped understanding how it “improves participants’ protection” and what it is its added value with respect to other models (by the way, which are the similarities, differences, added values vs the WHO guidance for ECs)?

- Concerning the SIDCER ICF templates, comparisons with other existing tools would have helped. For instance, which are the similarities, differences, added values vs the WHO informed consent templates?

- Concerning the “publication process as a gatekeeper against dissemination of unethical research”, it is not clear if it is also part of the FERCAP approach. This part is supported by two references only, dated respectively 2001 and 1996, but much more has happened meanwhile, for instance with the ICMJE taking strong stands on issues such as selective reporting (leading to registries) and more recently on data sharing. Importantly, here the authors completely ignore the current issues/debate about research integrity and, more specifically, around predatory journals.

On a formal note, breaking the text in sub-chapters would improve readability

Please let us know whether you would like your name to be published as a reviewer of the manuscript. No