TITLE: Who should participate in CHIMs and how should they be compensated?

Comments of Reviewer 1:

1. It would be useful if the introduction clearly illustrates the differences between clinical trials and CHIMs and why we need to consider participant selection and compensation differently in case of CHIMs.
2. The section on Motivation to participate is a very important and interesting section. The section begins with a statement that ideally, altruism should be the main motivator. This statement needs substantiation. Why should altruism be the motivator? What ethical reasoning supports this statement? This section goes on to describe the various motivations. What is the argument that supports that altruism is ideally the best motivating factor?
   1. The section on various factors motivating participation in the trials, it would be more readable if the motivating factors are grouped together like:
   2. Financial gains
   3. Treatment option
   4. Scientific interest / curiosity
   5. Access to good quality health care
   6. Trust in the researcher/physician

After such grouping, all the nuances of how this factor influences research participation and the different categories of this factor and their influence on trial participation can be described. This would make it more readable and understandable.

1. The statement that the motivating factors for participating in CHIMs is likely to be similar to that of other clinical research needs more substantiation. Why does the author think so?
2. The author should suggest how this can be achieved. How do we identify that the participant is purely motivated by financial gains.
3. Tables should be numbered and appropriately referred to in the text.
4. Also is there a scientific justification for excluding poor participants? If there is no scientific justification to exclude them, then shouldn’t we consider proper protection of the vulnerable – by ongoing close scrutiny.
5. Education and degree need not necessarily reflect health literacy and health related self efficacy. These need to be assessed.
6. In the table 2, the author has mentioned “access to health care” as a criterion for participant selection. This should be more clearly worded as “participants should have good access to health care”. This is also linked to socio-economic class and education levels.
7. Participants having the same goals as the researcher and altruism among participants is very challenging and difficult to assess and ensure. The author can give some suggestions for this.
8. Fair selection criteria have been described well. But some of them are in contradiction to the criteria specified in the table. One of the fair selection criteria is “people who bear the risks should also benefit from the research”. If middle and upper socioeconomic class participants are selected for the study, they will bear the risks, but infectious diseases are more likely to affect the poor and they will enjoy the benefits. Another criterion states that there should be a scientific basis for excluding certain groups of participants. What is the scientific basis for excluding the uneducated? Such conflicts have to be closely analyzed and reconciled.
9. A broader reflection on why these selection criteria are unique to CHIMs and may not be applicable to routine clinical trials needs to be justified.
10. It would be helpful to provide some more reflection on what the compensation should be. Should it be monetary? Can it be in the form of psychological counseling to handle prolonged periods of isolation, ensuring paid leave at work for participation in CHIMs, ensuring appreciation certificates of participation, honoring CHIM participants by giving them priorities in health facilities etc.
11. It would also be useful to reflect on compensation for side effects, adverse effects and injuries due to CHIMs.

*Comments of Reviewer 2:*

*1. The paper certainly addresses issues* *relevant to the fields of bioethics and medical ethics in the developing countries.*

*2. The authors have identified important issues concerning participant selection in CHIM studies and discuss critical issues around the same.*

*3.* *The issues around CHIM studies have been studied and expressed in various forms by many. However, the authors have summarized the issues with relevant literature to support and discussed the way forward in a cohesive manner.*

*4.* *The conclusions and proposed recommendations are grounded on the basis of the critique presented in the paper.*

*5. It may be useful to enlist the key issues and then present them one by one. Currently there is a need for improving clarity in the presentation of the issues (may be useful to use the same language in the presentation of the issues in the initial paragraph and when each issue is discussed) and the proposed three points (motivation for participation; selection criteria; and compensation) the discussion that follows. It may be useful to make consolidated table for the three points (point; sub-point; discussion/debate, recommendation).*

*6. It may be useful to restrict to CHIM-specific historical and ethical issues from studies and reviews on the same, rather than citing historically important ethics-related case studies which have been useful for general issues around ethical conduct of research*