Dholakia CHIM paper

REV COMMENTS

Comments of Reviewer 1 .

1. The introductory and descriptive section can be tightly edited and word count reduced. They are important and interesting facts and descriptions. But since it is a theme issue, some of this will be presented in other sections of the issue as well. The substantial content of the paper can start from the section “Does India need CHIM studies?”
2. A brief description of the reflective equilibrium approach, the method of reflective equilibrium approach followed in this analysis and the reason for adapting this approach to analysis can be provided.
3. The author refers to the Tuskegee syphilis experiment in the US. The Tuskegee experiment was not on normal human volunteers. This fact needs to be corrected.
4. The author uses the argument of a well- informed and understood informed consent to balance the fact that CHIMs are not to be worried about from an ‘emic’ perspective, provided such an informed consent is obtained. This argument needs more substantiation. A well informed and understood consent is the basis of protection of research participants even in the clinical trials and the vaccine trials that were problematic in India, which the author describes in the previous paragraph. The problem was that the informed consent was not truly well informed and protective. So, when informed consent did not really serve the purpose of protection of participants in those clinical trial and vaccine trial settings, how does the author argue that it will serve the purpose in CHIMs. In fact, in a previous section, the author does mention challenges in understanding as a factor which limits a fully informed consent in the Indian context. This needs to be reconciled.
5. The author quotes Evan and Evans. Do CHIMs fall under the category of non-therapeutic research where the harms are not more likely than those that one could meet in everyday life? This needs explanation.
6. The social value argument is a strong one. This can be elaborated more. Firstly, there is more scientific validity to the findings as it is done in the local endemic region to serve the people of a certain unique genetic and environmental characteristics. Secondly, the burden of infectious diseases, especially the emerging and re-emerging diseases is more in India and research should focus on these. It may even help balance the 90:10 gap in research in developing countries.
7. The argument that CHIM is a “fundamental need” needs to be built more strongly. This argument is based on an assumption that vaccine development for these diseases is a “fundamental need”. While there is strong evidence that vaccines are a successful public health intervention and certain vaccines have substantially reduced morbidity and mortality burden, this is not true of all vaccines. There are also vaccines of doubtful effectiveness. So the issue of vaccines as a “fundamental need” needs to be placed strongly. CHIM may be a fundamental need only for vaccines which can be proved to be a fundamental need.
8. The argument that basic sanitation and water supply are of same priority as “fundamental needs” as vaccines and CHIMs needs to be carefully considered. What makes these comparable priorities? How does the author argue that water and sanitation are not of more fundamental and basic value than vaccines?

**Comments of Reviewer 2.**

*1. Since an open, transparent discussion on whether the CHIM studies should be conducted in India is important even before active policy and legal framework can be defined, the opinions expressed in the article are relevant to thinking about policy.*

*2. There is a focus on India [emic] in the context of CHIM studies and a listing of etic issues as well. The paper is very topical.*

3. *CHIM as a subject/topic needs wider coverage and while this article covers many aspects which need attention and discussion of various experts and activists, it is good that IJME will cover additional aspects of CHIM studies in its special issue. Thus, while it is a somewhat specialised subject it certainly is a relevant topic.*  
  
*4. To the best of my knowledge, CHIM studies and their relevance in the Indian context has not been discussed much in the Indian academia or academic journals or lay press. For consumption of lay readers, health activists, ethicists together this article will provide food for thought.*

*5. The interpretation is valid and does not contain loose generalisations.*

*6. Whether in the current legal framework prevalent in the country CHIM studies can be conducted or not is an important point. Some reference to this complex issue, beyond an ethicist's view is desirable and has not been included.*

7. *The legal status of CHIM in India is not referred to. Thus, whether introduction of CHIM in India is simply an ethical debate or it needs a follow-up with regulatory/legal framework is an issue which is missing from this otherwise comprehensive article. It may be included.*

8. *The manuscript covers an important aspect of CHIM studies - why conducting CHIM trials is an ethical obligation. The author has covered many aspects of CHIM studies which contribute to the 'obligation' aspect, including etic and emic issues associated with it. Thus, the author emphasizes why despite other countries already conducting CHIM trials they should be conducted in India. The arguments are well made, many aspects are covered and appropriate background information and references have been provided.*

*9. While ethical obligations are clearly argued CHIM comes closer to Phase I clinical trial, though not quite identical. In this context what are the legal/regulatory issues which might create hurdles despite ethical obligation? Author could speculate about this point as it may be a potential practical challenge.*

**Reviewer 3:**

Some comments have been inserted into the text of the paper plus one comment below:

1. One thing I thought was completely missing was empowering Ethics Committees.

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