Title: **LAW AND ETHICS IN CONSENSUAL HARM DOING**

**Comments of Reviewer 1.  
General review comments:**

1.The paper presents a brief overview of the long-existing debate of human experimentations, law and ethics. The author identifies the relevance of the established issues of CHIM trials, within criminal law and ethics in Indian context.

2.Though it provides an interesting premise and problematizes the legal and ethical issues around CHIM trials, the author does not engage and discuss the existing debates and issues. The paper does not refer to established literature and studies which discuss these issues.

3.The author should make the objective of the paper clear and explicit. The overall analysis of the arguments of the paper does not provide sufficient evidence to reach the conclusion. For example, the conclusion section of the paper just restates the statements without providing clear analysis in the previous sections: the discussion about regulations and regulatory mechanisms in India was not at all addressed

**Specific comments:**

Please add an Abstract. It would be very helpful for the readers.

**Introduction:**. It would be helpful if the author provides the aim or focus of the paper explicitly and focuses on one major or few themes and constructs the arguments accordingly. For example, “this article measures some of these legal and ethical challenges raised in CHIM trials”, Please mention that there is not much legal or ethical discourse on this subject, specifically in India.

“What about the legal and ethical obligations of the researcher “to do no harm” (non-maleficence) to research participants?” Can we, for the sake of advancement of science, justify exposing individual research participants to harm by infecting them with a disease? Do individuals have a right to submit themselves to harm, even though it may be in a controlled setting, and minimal? Can taking informed consent for intentional harm or for taking such a risk of harm, nullify the harm doing? This article measures some of these legal and ethical challenges raised in CHIM trials.”

These above questions raised by the author have been frequently mentioned and debated in law and ethics, especially within human experimentations. It would be useful to refer to some of the literature in the discussion.

**The Harm Principle**

Though the summary of Mill’s and Feinberg ’s argument is provided, I do not see the author’s analysis or arguments. For example, would you give significance to the Harm principle and why within the Indian context?

Would you state then the “informed consent forms of CHIM trails are invalid?” If Yes, then how do you arrive at this statement. If No, then, what ethical issues would be pertinent and how would you present your analysis in this section?

For example, what is your analysis of how the law should act and enforce “consent” in CHIM trails?

Page 5: “The magnitude of the harm would also need to be measured to make consent relevant in CHIM trials.” Please provide details on how one could measure the harm in CHIM trails. Given the present evidence that harm of CHIM trails are low in India and generally, then would you state the higher the harm, consent is irrelevant and lower the harm consent is relevant? Then the question would be is the intrinsic value of consent completely dependent on the magnitude of harm? If so, how would you justify the moral significance of consent within CHIM trails?

**Compensation**

“The WHO guidance document states that the information gained should clearly justify the risks to human participants and that “it is essential that challenge studies be conducted within the ethical framework in which truly informed consent is given”(i). The qualification of “truly” informed consent seems to suggest that informed consent taken for clinical trials is not truly informed consent, which is required for CHIM trials.” This statement and analysis are not clear and detailed. Please provide your analysis on why you are critical of “truly” informed consent. The reader would be needing further details.

“But, is informed consent enough to allow CHIM trials? There does not appear to be much documentation on the high amount of compensation given to healthy participants to enroll for CHIM trials.” You have not provided any evidence (through reports or papers or cases).

Again, it seems you are asking rhetorical questions, “would provide high compensation be an inducement for persons to take the risk of harm? What is the true meaning of respect and dignity of the individual human participant, who agrees to be harmed and to take the risk of harm for the sake of science and is then faced to battle with temporary or reversible harm or permanent harm?” It would be insightful if you could first provide enough details and analysis before raising concerns. Also, provide your positions and arguments.

**Some suggested readings**

Emanuel, E. J., Wendler, D., Killen, J., & Grady, C. (2004). What makes clinical research in developing countries ethical? The benchmarks of ethical research. *The Journal of infectious diseases*, *189*(5), 930-937.

Emanuel, E. J., Wendler, D., & Grady, C. (2000). What makes clinical research ethical?. *Jama*, *283*(20), 2701-2711.

Resnik, D. B. (2003). Exploitation in biomedical research. *Theoretical medicine and bioethics*, *24*(3), 233-259

Resnik, D. B. (2015). Unequal treatment of human research subjects. *Medicine, Health Care and Philosophy*, *18*(1), 23-32.

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**Comments of Reviewer 2**:

The author asks some very pertinent questions in the third paragraph. She asks whether it is right to expose individuals to risk of infection in order to advance science? Whether individuals have the right to subject themselves to harm? Can taking informed consent, permit subjecting an individual to intentional harm etc. I am also simultaneously thinking of the following questions:

1. Phase 1 drug trials on healthy volunteers is also a form of consensual harm. Would the concepts in this paper apply to them also?
2. There are some public health interventions like vaccination, mass drug intake by all people in order to eliminate a specific disease etc, where many healthy individuals consent to subject themselves to a “harm” of adverse effects of the vaccine and drugs for a probable benefit for themselves and a collective benefit to the community. Would these arguments apply to them too?

I think the author should address these too.

The concept that controlled human infection is actually harm should be established strongly. The author has to clearly argue that even though the infection is “controlled”, even though it is attenuated and not virulent, even though the volunteers are isolated and closely monitored, even though there is a good treatment readily available to reverse the problems, the infection is “harm”. She can argue this based on uncertainty in behaviour of even avirulent infective organisms, irreversibility of some of the symptoms and harms in some cases such as Zika virus, etc.

The author refers to Section 269 and 270 of the IPC, Would this law apply if the researcher believes it to be incapable of causing serious harm to life? Would it apply if the researcher believes that he/she has taken all precautions to limit its spread and is closely watched by an oversight committee?

It would be helpful if the author can describe that there is no imminent need for a CHIM. The more immediate need is for strengthening of primary health care and social determinants of health, which are more basic rights of every human being.