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Ethics Mentor Report

October 26, 2021

Inês Fronteira (co-PI), met via zoom with the Ethics mentor, Prof. José João Abrantes, to present the study and current situation.

November 8, 2021

Inês Fronteira (co-PI) contacted the Ethics mentor, Prof. Jose Joao Abrantes, by e-mail to present the bellow described question and to ask for his position on the mater:

"As mentioned in a previous conversation, we had initially set the minimum number of participants for the study at 1050 participants, 350 distributed by each of the countries (Cape Verde, Guinea Bissau, and Mozambique). The refusal of permission to implement the study in Cape Verde meant that we had to distribute the participants from this country to the others, i.e. 525 in Guinea Bissau and Mozambique. The successive delays in the implementation of the study, such as those related to the authorizations from ethics committees and other bodies, as well as difficulties experienced already during implementation (e.g., vaccination process for COVID, strikes of health professionals, etc.) led to the predictable impossibility of reaching the minimum number of participants by December 17, 2021, the date on which the recruitment of participants ends. We currently have 675 participants in the study, and it is anticipated that we will be able to reach approx. 750 by the deadline.

In this regard, the funder has raised the issue that it is not ethically acceptable to recruit more participants (which means stopping recruitment now) as their number would not be powerful enough to demonstrate a difference in days of absenteeism for COVID between those vaccinated with BCG and those vaccinated with the placebo.

After consultation with the Data Safety Management Board of the project, as well as the larger project team, we believe that while this may indeed be the case, there are other relevant outcomes that may benefit from including as many participants as possible, namely, incidence of COVID (having or not having the disease) and unplanned absenteeism for infectious diseases other than COVID. Furthermore, it seems to us that there is a moral obligation towards the already recruited study participants to try to recruit as many people as possible so that their participation is not futile.

In light of the above, I would like to ask you to advise us, as the project's ethical mentor, regarding the ethically recommendable position."

We hereby present the answer given by the Ethics mentor, by email, on November 11, 2021:

"… your message pointed out very well the different vectors that intersect in this problem. I think that this, contrary to what the funder maintains, is not so much an ethical issue. If the fact that the number of participants does not enable the study authors to demonstrate the differences, in terms of absenteeism due to COVID, between those vaccinated with BCG and those vaccinated with the placebo, may be relevant, it is the study authors themselves who, after consulting the

Data Safety Management Board of the project and while accepting the possibility of this risk, state that "there are other relevant outcomes that may benefit from the largest possible number of participants, namely, incidence of COVID (having or not having the disease) and unplanned absenteeism due to infectious diseases other than COVID". This is a compelling argument, decisive, in my opinion, to remove any ethical objection."