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We thank all our commentators for engaging so encouragingly with a proposal that many would regard as simply too radical to consider seriously pursing in practice. In the spirit of encouraging further debate and developing our proposal further, we respond to their lines of inquiry by addressing five kinds of criticism.

The first criticism questions the likelihood that the vaccine experiments will produce benefits either for apes or for humans. Specifically, Addison and Malone (2018) question the value of nonhuman primates as models for human biology and point out that the Ebola virus mutates often, so the "suitability" of any vaccine is questioned. The value of vaccine development generally, however, seems to be supported by the use of ring vaccination with Merck rVSV, in humans known to have been exposed to the Zaire strain of Ebola, implemented twice already during 2018 in separate outbreaks in the Democratic Republic of Congo. Its longevity and efficacy as an intervention are indeed yet to be determined; we see this as another reason to pursue a pipeline of different approaches to find out. More ecological and sero-prevalence work is needed to discover the natural reservoirs of Ebola virus (Afolabi and Afolabi 2018), but more surveillance is helping predict how outbreaks will spread and where future outbreaks are likely. The EcoHealth Alliance's PREDICT program continues to help in this regard.

The flip side of the first criticism, the second kind of criticism suggests that the experiments with wild apes are riskier than we let on. For example, Addison and Malone (2018) say that it is unclear how well administration of the vaccine could be realized by noninvasive means, that risk factors may interact, and combined pose a greater risk than each taken independently (experiment too risky). Human involvement in experimental vaccine administration and observation could have foreseen and unforeseen negative consequences. More human encounters with apes might decrease the apes' fear of humans and lead to more human–ape encounters, and maybe more Ebola. Furthermore, the vaccine may negatively impact target species either through vaccine-related effects or through stress (Gruen 2018).

Whether or not the potential benefits outweigh the very real risks in this experiment is up for debate. The commentaries have identified risks and benefits that we had not previously considered, and these and others should be seriously considered if proposals like the one we discuss go forward. One thing to consider even before making this assessment is whether we think of risk as a threshold requirement or relative requirement. By this we mean: Do the risks cross some threshold (such as violating animals' rights or integrity) such that no amount of benefit would justify risk exposure? Or, should we ask instead: Do the risks outweigh the benefits? One's answer to this question informs the analysis. If we think of risk as a threshold requirement, we will argue that no amount of benefit is enough. If we think of risk as a relative requirement, we will think that the benefits must outweigh the risks. This means that

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despite the very real risks of moving forward with this proposal, these are outweighed by potential benefits, and, all things considered, it is permissible to move ahead. We would not want to take sides here, only to make a further point about the relationship between benefits and risks in the moral evaluation of animal research.

The third kind of criticism lies in our apparent inattention to other ways of mitigating the risk of Ebola to apes and humans, especially those that highlight humans' role in increasing infectious disease risks, like deforestation, hunting, and anthropogenic climate change (Addison and Malone 2018; Gruen 2018). Nothing in our proposal or analysis supports either the assertion that vaccine development is the only way to mitigate risk of Ebola for apes and humans, or the assertion that it is the best way of doing so. We fully agree with the commentators that other, more ethical and effective, ways of mitigating Ebola risk ought to be seriously considered, and, if practically and politically feasible, pursued in our common goal of mitigating the risks of infectious diseases. We have no doubt that understanding and making incremental progress toward alleviating deforestation, urbanization, the need for hunting, and other problems would likely have an impact on Ebola transmission—not to mention mean that more humans' and animals' rights would be respected, that more people would lead dignified lives. At the same time, vaccines may be part of the Ebola-reduction strategy, one that might offer quicker and more politically acceptable solutions to the global ecological problems of our age. Addressing the myriad issues that contribute to infectious diseases may provide an overall greater net benefit. But we don't know that. Might vaccines provide benefit? The point of our article is: Should we even do the experiments to find out? We argued that we should.

The fourth kind of criticism suggests that our proposal is insensitive to power dynamics and the importance of partnership in the vaccine development and risk management process. While our proposal did not explicitly account for local involvement in the design of the research, or in the decision to go ahead with it, we agree with commentators that this should happen. Being aware of the power dynamics, political concerns, and legal mandates for decision making is incredibly important. Under International Health Regulations, national governments are advised by the World Health Organization in the preparation of human outbreaks. Vaccine developers are always going to be concerned with, if not entirely motivated by, profit (Afolabi and Afolabi 2018). The best we can do is to hold them accountable to and encourage consideration of competing interests. In the context of experiments with wild apes, other stakeholders, local, regional, and international, will also need input. For example, the World Conservation Society continues to engage with indigenous hunter-gathering communities to help estimate the numbers of gorillas and chimpanzees killed for food, out of which the numbers of apes exposed to the Ebola virus can be determined from donated carcasses. Radical behavior change of hunter gathers may be unlikely in the near future, but local community engagement is already being tested through ongoing human trials of vaccines and now of treatments, as well as through ecological sero-prevalence studies in animals and humans.

The fifth kind of criticism we see as deepening our theoretical understanding of the One Health framework, rather than opposing our proposal as such. We thank Lederman and Capps (2018) for articulating the One Health ethic perhaps more deeply than we did, and for the prior work on which we drew for the article. They offer important theoretical considerations about how we should conceive of the ultimate good we are aiming for in developing a public health ethic, an environmental ethic, or a research ethic. Is it "the greatest good for the greatest number of creatures" or "universal goods" or something else altogether? Although this may not matter much to the defense of the proposal, it matters a lot to framing the issue and articulating a common purpose and goal that unite public health and environmental ethics in a really beautiful way.

In closing, we hope that any experiment that goes forward will do so cautiously, carefully, and with eyes wide open about foreseeable consequences. On the other hand, respecting all partners in the experiment (humans and animals) also means stopping if foreseeable negative consequences and unjust risk/benefit arrangements are unavoidable. We remain open to both of these possibilities. The best we can hope for is that the approach explored in our article chips away at what Dr. Rollin so nicely articulated: "the cavalier disregard we display for the lives and, more importantly, the quality of lives of those creatures upon whom we depend in so many ways" (Rollin 2018). We couldn't have put it better ourselves. ■

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