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LETTERS

RESPONSE

# Miles W Carroll replies to Deborah Cohen

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Cohen discussed a study performed at the Health Protection Agency, now Public Health England, in her article about vaccine research and the role of preclinical studies.[1] Public Health England has responded to all requests for information about this study, but in the interest of clarity and transparency in animal research we would like to make the following comments.

Animal studies at Public Health England are conducted to extremely high standards. They were and continue to be compliant with the UK Animals (Scientific Procedures) Act 1986 and the EU Directive 2010/63/EU. The study in question was designed and conducted in accordance with these regulations, and the aims and all experimental details of the study are openly stated in the 2010 publication.[2] Suggesting that this tuberculosis model development study was conducted as a preclinical trial to support the progression of vaccine MVA85A to human trials is incorrect.

Cohen's article says that, "although the difference between the BCG and MVA85A groups wasn't statistically significant, the Porton Down study gave a strong signal that the MVA85A vaccine was hastening the development of TB in the macaques, raising the possibility that MVA85A was actually impairing the effectiveness of BCG." There was no evidence from any read-out used in the study to support the claim that the group vaccinated with MVA85A developed progressive disease more rapidly.

As outlined in the original publication,[2] it was the first attempt to develop a new model for vaccine assessment using aerosol challenge. Our work was published after careful analysis of all study parameters and without any delay after analyses had been concluded on material from the macaque study. This was completed in 2009. We were unable to discriminate survival outcomes among the groups, but the pulmonary disease burden was significantly lower in animals vaccinated with BCG alone or with BCG boosted with MVA85A than in the unvaccinated control group when measured by a new and more sensitive read-out of disease using advanced imaging.[2] In the years after completion of this initial exploratory study, the design of the macaque model has been further refined.

Competing interests: None declared.

1 CohenD. Oxford TB vaccine study calls into question selective use of animal data. BMJ2018;360:j5845. doi:10.1136/bmj.j584529321165

2 SharpeSAMcShaneHDennisMJ. Establishment of an aerosol challenge model of tuberculosis in rhesus macaques and an evaluation of endpoints for vaccine testing. Clin Vaccine Immunol2010;17:1170-82. doi:10.1128/CVI.00079-1020534795



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