Author's response to reviews

Title: Persistence of the humoral and cellular immune response of an H5N1 adjuvanted influenza vaccine in elderly persons: two-year follow-up of a randomised open-label study

Authors:

Paul Gillard (paul.gillard@gsk.com)
Didier Giet (d.giet@ulg.ac.be)
Stéphane Heijmans (stephane.heijmans@researchlink.be)
Mamadou Dramé (mamadou.x.drame@gsk.com)
Karl Walravens (karl.x.walravens@gsk.com)
François Roman (francois.x.romans@gsk.com)

Version: 2
Date: 5 November 2013

Author's response to reviews: see over
Dear Professor Altman,

Please find enclosed the manuscript entitled “Persistence of the humoral and cellular immune response of an H5N1 adjuvanted influenza vaccine in elderly persons: two-year follow-up of a randomised open-label study” for your consideration for publication as a research article in *Trials*.

The reduced immune response to influenza vaccination seen in elderly persons may be improved by administering a higher vaccine dose. We therefore assessed the immune response to 2 double doses of an AS03₃₃-adjuvanted H5N1 vaccine (7.5 µg hemagglutinin) and to 2 single doses of this vaccine (3.75 µg hemagglutinin) in persons above 60 years of age. We previously reported that, while 2 injections of the double dose induced a stronger immune response, 2 injections of the single dose were sufficient to meet licensing criteria (Heijmans S et al. *J Infect Dis* 2011; 203(8):1054-62). We now report that persistence of the antibodies was observed up to 2 years after vaccination for both regimens, with no difference observed between the two regimens. However, we did observe improved antibody persistence in the groups receiving AS03₃₃-adjuvanted vaccine compared to non-adjuvanted groups.

Our findings indicate that there is no need for increased doses in elderly individuals for this adjuvanted influenza vaccine. This knowledge can thus simplify the vaccination schedule across adulthood. Moreover, it reduces the strain on the limited global production capacity of influenza antigen in case of a pandemic.

The manuscript has been solely submitted to *Trials* and has not been previously published.

I suggest the following potential reviewers:
Menno D. de Jong ([m.d.dejong@amc.nl](mailto:m.d.dejong@amc.nl)) has published extensively on H5N1. Woo-Joo Kim ([wjkim@korea.ac.kr](mailto:wjkim@korea.ac.kr)) has published on the subject of influenza antibody persistence in the elderly. Marc van Ranst ([Marc.Vanranst@uzleuven.be](mailto:Marc.Vanranst@uzleuven.be)) is a virologist based in Belgium, where the study was conducted. There is one publication in *Retrovirology* where Marc van Ranst is co-author with Francois Roman, but this publication has about 250 authors.

Thank you for considering our manuscript for review. We look forward to hearing from you.

Sincerely,

Paul Gillard
paul.gillard@gsk.com