Reviewer's report

Title: A phase II, open-label, multicentre study to evaluate the immunogenicity and safety of an adjuvanted pandemic (H5N1) influenza vaccine in healthy Japanese adults

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Reviewer: Jinxia Zhang

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This paper entitled “A Phase II, open-label, multicenter study to evaluate the immunogenicity and safety of an adjuvanted pandemic (H5N1) influenza vaccine in healthy Japanese adults” by Hideaki Nagai, Hidyuki Ikematsu, Kazuyoshi Tenjinbaru et al reported a clinical study on the safety and efficacy of a H5N1 influenza split-iron vaccine adjuvanted with AS03A in a Japanese population. The study was conducted in two centers with 100 healthy individuals aged from 20-64 years. After the second dose of vaccination, the seroconversion rates and seroprotection rates, in terms serum HI antibody titer against vaccine strain (A/Indonesia/5/2005) reached 91%. The serum HI antibody also showed substantial cross-reactive to other H5N1 stains. During the whole period of study, there was no serious adverse effect found. The authors concluded that the vaccine is safe and elucidates high humoral immune response against vaccine strain H5N1 virus in this Japanese population.

On the whole, this is a well designed clinical study and the data here have provided sufficient information to support the authors’ conclusion. I would therefore recommend that the article can be accepted for publication in the journal of BMC Infectious Diseases provided that the following points are required to be clarifications or explanation by the authors before publication.

1. (Minor Essential Revisions) Since the first appearance of H5N1 in 1996, this subtype of influenza virus has evolved into multiple clades in terms of their HA gene. Theoretically, virus from any of this clade could be a candidate to cause pandemic. So, I think the use of “pre-pandemic vaccine” in this article seemed misleading. It would be more appropriate just to use “H5N1 vaccine”.

2. (Minor Essential Revisions) WHO has to update the vaccine strains every year for seasonal H1N1 and H3N2 influenza due to the rapid evolutionary rate of influenza virus. So, in the Discussion, the authors should provide some information on how much the H5N1 subtype of influenza virus has been evolved in recent years, especially their HA genes. Because the vaccine strain used was an isolate of year 2005, it would be helpful for the authors to explain the pharmaceutical value of a vaccine which produced from a viral isolate five years ago.

3. (Minor Essential Revisions) Horse red blood cells and chicken red blood cells were used in HI and MN test respectively, is there any specific reason for using
difference type of RBC in these two tests?

4. (Minor Essential Revisions) Page 9 line 22 to line 26 “A cell suspension, containing a defined number of MDCK cells were then added to the mixture of virus and antiserum and incubated at 33C....” From this description, I found it difficult to understand the rational how the MN assay was performed. It would be helpful if the methodology on MN assay to be explained in more detailed.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests