Reviewer's report

Title: A randomized, controlled non-inferiority trial comparing H1N1 2009 pandemic vaccine antigen, with and without AS03 adjuvant system, co-administered or sequentially administered with an inactivated trivalent seasonal influenza vaccine

Version: 1 Date: 24 January 2012

Reviewer: Zol Vaj

Reviewer's report:

The topic is of interest, although several publications have addressed this issue before. One of the major weaknesses of this study is the lack of any patients over 40 years of age.

Methods
In the "Study Vaccine" section, an error message is seen in the text: "error, reference not found".
I see no allocation concealment mechanism.
It is not reported who generated the allocation sequence, who enrolled participants, and who assigned participants to interventions?
Were the adjuvant really mixed with the vaccine on the day of vaccination by a nurse? This does not seem to be GMP compliant. How was the quality and accuracy assured? I see that the ratio was 1:1 but what volumes were used? Was this an FDA approved method?
Was the mixed product, containing the adjuvant, similar in appearance of the non-adjuvanted vaccine? How about the appearance of the placebo?
The TIV used in the trial is not with the approved strains for the 2009-10 season, which were the A/Brisbane/59/2007 (H1N1)-like virus, the A/Brisbane/10/2007 (H3N2)-like virus and the B/Brisbane/60/2008-like virus. Why did the investigators use a vaccine that was not approved for the season when the study was conducted?
The subject numbers in each group (85-92) seem to be too low to prove non-inferiority.

Results
The baseline demographic and clinical characteristics should be reported, preferably in a table.
Reasons for not vaccinating more than 250 enrolled subjects are not provided.
The rate and severity of reactions seem to be excessive with the adjuvanted formula: >90% for reactions and over one third of the subjects required medical visits due to reactions - this vaccine cannot be described as "well tolerated".
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests