Reviewer's report

Title: Extended antigen sparing potential of AS03-adjuvanted pandemic H1N1 vaccines in adults and children: Results from two randomised trials

Version: 3 Date: 17 June 2013

Reviewer: Helen M Oh

Reviewer's report:

1. The questions posed by the authors are well defined. In the background section, the authors had explained the importance of providing reassurance on the comparability of the 2 formulations D-Pan and Q-Pan H1N1 by demonstrating immunological equivalence between the 2 vaccines.

2. The methods for both the adult and children studies are appropriate and well described especially the end-points for the immunogenicity i.e. seroconversion rate and seroconversion factor.

3. The data are sound, clearly stating the criteria to meet the primary objectives. In fact the immunogenicity in adults and children exceeded CHMP and CBER regulatory acceptance criteria.

4. Yes, the manuscript does adhere to the relevant standards for reporting and data deposition.

5. The discussion and conclusions are well balanced and adequately supported by the data. The pediatric data demonstrated the reduction of HA dose resulted in a strong immune response in children as well as antibody persistence 6 months post vaccination. The implication of the antigen sparing potential of ASO3 adjuvant is to allow an increase in the number of doses from available antigen bulk.

In discussing the reactogenicity and safety profile of Q-Pan and D-Pan, the authors also mentioned the reports on the increased risk of narcolepsy in children and adolescents vaccinated with Pandemrix in Europe. Their data on adverse events in adults (Germany and France) and children (Philippines and Thailand) did not reveal any case on narcolepsy or Guillain-Barre syndrome.

Discretionary revision: Include stronger references for risk of narcoplepsy in children and young people receiving ASO3 adjuvanted H1N1 vaccine –


6. The limitations of work were clearly stated by the authors for the age group 10 to 18 years which was not studied in the two randomised trials. They did provide several relevant references for the immunogenicity data for this age group. However, the authors should have discussed the importance of evaluating the immunogenicity of AS03 adjuvanted H1N1 vaccine in older adults (age > 65 years). Obviously more studies need to be done to evaluate the immunogenicity
and safety of adjuvanted H1N1 vaccine in this age group.

Discretionary revision: One additional reference for the use of ASO3 adjuvanted H1N1 vaccine in children is Langley JM et al. The Ped Infect Dis J 2012;31:848-58.

7. The authors acknowledged the need to investigate the possibility of further reduction of the antigen dose to children.

8. The title and abstract does not accurately reflect what has been found in this study. The objectives stated in the manuscript in the last sentence of the background section are correct.

Major Compulsory revision: Title - Extended antigen sparing potential of ASO3-adjuvanted pandemic H1N1 vaccine in children and immunological equivalence of 2 formulations of ASO3-adjuvanted H1N1 vaccines: Results from 2 randomised trials.

Abstract conclusion - …… different HA doses elicit an adequate immune response through 180 days post vaccination in children (aged 3 – 9 years).

9. The writing is acceptable.

**Level of interest:** An article of importance in its field

**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.