Reviewer’s report

**Title:** Safety and Immunogenicity of a freeze-dried, Vero cell culture-derived inactivated Japanese encephalitis vaccine (KD-287, ENCEVAC(R)) versus mouse brain-derived inactivated Japanese encephalitis vaccine in children: a phase III, multicenter, double-blinded, randomized trial

**Version:** 1  
**Date:** 2 April 2014

**Reviewer:** Akihiko Saitoh

**Reviewer’s report:**

This is a relatively straightforward phase III, double-blinded, randomized study evaluating the safety and immunogenicity of a Vero cell culture-derived inactivated Japanese encephalitis vaccine vs. mouse brain-derived inactivated Japanese encephalitis vaccine in Korean children. Subjects were 205 healthy Korean children aged 12-23 months. Each subject received either Vero cell culture-derived inactivated vaccine or mouse brain-derived inactivated vaccine twice at an interval of 2 weeks followed by 12 months booster vaccination. After the three doses, Vero cell culture-derived inactivated vaccine was safe and had high immunogenicity with the seroconversion rate of 100% and no inferiority was observed compared to mouse brain-derived inactivated vaccine. They concluded that this is the first study to compare the safety and immunogenicity of a Vero cell culture-derived vaccine vs. mouse brain-derived inactivated vaccine in Korean children and the Vero cell culture-derived vaccine can be substitute for the current mouse brain-derived inactivated vaccine because of its lower potential risk of serious neurological adverse reactions and sufficient vaccine supply.

Overall, this manuscript is well written and demonstrated the safety and immunogenicity of Vero cell culture-derived inactivated Japanese encephalitis vaccine in Korean children. There are some issues need to be addressed after this reviewer read the manuscript.

**Major Compulsory Revisions**

1. **Page 10**
   
   No description of statistical methods was noted in this section. This needs to be stated in this section.

2. **Page 30-33, 35, Tables 1-4, 6**
   
   The Fisher’s exact test was used for the comparison of numbers of subjects throughout the study. What was the reason why the authors did not use Chi-square test?

3. **Page 30, Table 1**
   
   The age was described as mean ± SD. Are these normally distributed?
What is the reason why the rates of concomitant medications are so high?

Minor Essential Revisions

1. Page 8, Line 16
   Please describe in details regarding “reported passively during a telephone interview”. Did the authors call for all guardians or parents after the vaccination to interview?

2. Page 10, Line 15
   What does PP stand for?

3. Figure 1
   First box on right, reason
   Not received any vaccine should read “Received any vaccine”.

The JEV-GCC (N-102) should read JEV-GCC (N=102).

4. Figure 3
   It is very difficult to distinguish from each blue and red line. Please describe or add arrows to clarify.

Discretionary Revisions

1. Page 8, Line 3
   A regular interval for inactivated vaccine for primary series is usually 4 weeks. What is the reason this was set for an interval of 2 weeks?

2. Page 21 Line 14, Page 32, Table 3
   Although the authors described nasopharyngitis was not directly related to vaccine, what is the reason why the incidence of nasopharyngitis is so high up to 80%?

3. Page 33, Table 4
   What is the definition of pneumonia? Why the incidence of pneumonia is so high in both populations?

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I declare that I have no competing interests.