Reviewer's report

Title: Frequency of apnea, bradycardia, and desaturations following first
diphtheria-tetanus-pertussis-inactivated polio-Haemophilus influenzae type B immunization in
hospitalized preterm infants

Version: 3 Date: 3 April 2006

Reviewer: Jukka Jokinen

Reviewer's report:

General

Major Compulsory Revisions (that the author must respond to before a decision on publication can
be reached)

1. case-controlled study

In their most recent reply, the authors argue that the term control group is
appropriate, which is OK by me. However, they have ignored the arguments in my
two previous reviews regarding the misleading case-control terminology. In this
typescript, the authors use the term 'a case' for a child that has been
vaccinated. However, the vaccination is the exposure variable in this study.
Since 'a case' in medical literature refers to a subject with the disease in
question, it is inappropriate to use it to describe the vaccinated. Please
remove all references to cases and refer to this particular group as immunized,
vaccinated, or something equivalent.

For the remainder of this review, I will use the term 'vaccinated' for the
children that are referred to as 'cases' in the typescript.

2. immunization in the control group

On p.10 r.13-17 the authors now state that almost all control infants were
already immunized or were eventually immunized (often prior to discharge). The
reader is now easily confused: On p.5 r.1-7 the authors state that these
control infants were selected during the same follow-up period as the
vaccinated, were of same gestational age, and were not yet discharged from
NICU. If they fulfilled the eligibility criteria of the vaccinated stated on
p.4 r. -3-1, why were they not included in the group of vaccinated? Presumably,
these control children that were already immunized were a subgroup of those 60
children that were excluded from the group of vaccinated because of exclusion
criteria (p.6 r.-3-1). This implies that at least 64 control infants were
vaccinated after discharge. Please provide a specific description of how many
of those 60 that were excluded from the group of vaccinated were included in
the group of controls, how many control children had their vaccination after
discharge, and also how the information regarding their vaccinations after
discharge was obtained. The vaccination information is absolutely essential
when determining the characteristics of the vaccinated and the control group,
and deserves a thorough and detailed description in the typescript.
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

p.4 r.9-11: 'However, none of these studies included a control group ... so the relationship between the immunizations and these events has not been clearly established.'

If none of these studies included a control group, to what were they compared to? If the comparison was done by using the subject itself as a control, this comparison is actually a preferred way compared to the approach suggested by the authors (as they state on p.10 r.11-12). Therefore if the authors intend to include the statement 'the relationship has not been clearly established', this requires a more thorough argumentation.

p.4 r.14: 'A case controlled retrospective study'

Please delete all references to case controlled studies. The study design in this typescript is a retrospective stratified cohort study.

p.6 r.10-11: 'Categorical values were compared by chi-square and cells with small contents by Fisher's exact test.'

I can only find one test result on p.7 r.-3. Please modify the sentence by stating specifically that the cellular and acellular vaccines were compared by using this method. Also state that which one (Fisher or chi-square) was used.

p.6 r.14: 'Differences were considered statistically significant for values of p<0.05'

Please include a statement that if the 95% confidence interval of the odds ratio did not include the value one, the difference was considered statistically significant.

p.10 r.7-8: 'the use of matched controls should decrease the effect of multiple nurses performing the observations'.

The authors have not stated that the controls were also matched according to the nurse performing the observations. In other words, if the control child was not observed by the same nurse as the vaccinated, this possible confounding factor is still present in this study and therefore this sentence should be removed.

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Acceptable
Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests