Reviewer’s report

Title: Folic acid supplementation before and during pregnancy in the Newborn Epigenetics Study (NEST)

Version: 1 Date: 22 July 2010

Reviewer: Della Forster

Reviewer’s report:

Thanks for the opportunity to review this paper. The question of ‘how much folic acid is too much during and prior to pregnancy?’ is an important one.

I have some comments and questions on the paper; all of which I consider require revision or response.

Introduction:
This section seems fine, and covers the relevant content that is being explored in the paper.

Methods:
1. NC is not defined, and those outside the US will not know what it means.

2. The paper would be improved by more information on how the recruitment was undertaken, and by whom. As it is currently written the reader cannot assess the rigour of this important aspect of the study. It is also unclear what inclusion and exclusion criteria were applied.

3. As the paper goes on, it becomes unclear what is really being included in the analysis. There is quite a lot of detail about what data is collected and how (although we are not told if serum folate was undertaken, and if not why not given the study questions), but it seems to become evident that it is only folic acid supplements that are actually being discussed and presented in this paper. Is that correct? Or are the dietary intakes also being converted into intake and included? This all needs to be much more transparent and the reader talked through it logically. I was assuming that given the dietary intake data collection was described then this was included, then I came to the section where there is a ‘no supplement’ group, leading me to think then that this was the only aspect included. If so, then the dietary intake aspects could be omitted. The only thing I can see in relation to that is the sentence about the correlation doses and total folate reported, but I am not sure what this means. If this information is retained it would need further explanation, and possibly belongs in the results section.

4. The data analysis description says that there was mutual adjustment in the regression models to arrive at parsimonious models, but as far as I can see only univariate ORs are presented. Is this correct? If so, then why is this? If this is not correct, then the results as they are need to be written in a way that increases
clarity. I would think if multivariate analysis has been undertaken this should be the results that are presented. I am not sure of the value of unadjusted ORs being presented as the main finding.

**Results:**

5. In presenting the results on the proportion of women who took above the upper recommended dose of folic acid, we are given no information on these women. Are some of them in fact in groups where a higher supplement would be recommended, e.g. family history of neural tube defects or women who are obese. Presenting only the proportions without some attempt to look at this may be misleading.

6. In the section on pre-pregnancy and pregnancy-related FA supplementation, I found the fourth sentence confusing – the % of women reported here i.e. 6% and 13% did not seem to equate to the % reported just above. This section may need some re-writing or clarification.

**Discussion:**

7. The discussion starts off with a sentence about the proportion of women who reported taking 400 micrograms or more of folic acid per day, yet the results focus on 1000 micrograms or more per day. This could be considered when revising the paper as the reader has no way of verifying that statement based on the data presented.

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

**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'