Reviewer's report

Title: Nitric oxide synthase 2A (NOS2A) polymorphisms are not associated with invasive pneumococcal disease

Version: 1 Date: 17 February 2009

Reviewer: Stephen J Chapman

Reviewer's report:

Major Compulsory Revisions
1. Nil

Minor Essential Revisions
2. Spelling of ‘asymptomatic’ in abstract, background.
3. Background, second paragraph, reference 10 in fact describes an association between IPD and members of the ‘inhibitor of NF-kappaB’ family NFKBIA and NFKBIE, not NF-kappaB itself.
4. Table 2, ‘95% CI’ – presumably of odds ratios?

Discretionary Revisions
5. Table 2, the genotypes presented appear to pool the cases and controls and survivors/non-survivors for each snp, might be more informative if presented these separately. The MAFs for cases and controls in table 1 allow easy comparison.
6. Case definition. Some experts would not consider pneumococcal pneumonia in the absence of bacteraemia to be ‘invasive pneumococcal disease’, the authors may wish to expand upon this – although I appreciate that in the very least the phenotypes are very closely related and the distinction may simply reflect blood culture practice or timing. In any case it is highly unlikely to alter the conclusions of the paper.

Conclusions
7. A comprehensive and well-written assessment of a biologically plausible candidate gene for IPD susceptibility and outcome. Although a negative study, it is well-designed and executed and draws appropriate conclusions. As such the study adds to the overall body of knowledge on this subject and I would recommend publication.

Level of interest: An article whose findings are important to those with closely related research interests

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