Reviewer's report

Title: Age-adjusted Plasmodium falciparum antibody levels in school-aged children are a stable marker of microgeographical variations in exposure to Plasmodium infection

Version: 1 Date: 30 March 2007

Reviewer: Chris Drakeley

Reviewer's report:

General
This MS by Wilson et al reports on associations between antibody levels to crude malaria parasite extract and proximity to potential malaria vector breeding sites. The authors suggest that age adjusted IgG3 levels in school aged children have potential in mapping the local variations in malaria transmission. The MS is well written and well presented and is a logical continuation of their previous work (Booth et al 2004). There are a few methodological issues I think need to be addressed and subsequent caveats explained in the discussion before it should be published.

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

1. Methods: there is no reference for Pf antigen prep. The laboratory strain in particular has some relevance as it may not be 'local'.
2. Methods: Are there any correlations available for sera from separated blood versus that from filter paper? I know this method is widely used in neonatal studies but has it been described for malaria. What was the serum dilution from a 6mm disc (diameter, radius, volume?) and final dilution in the assay. This is not in the Booth paper and I do not have the JID paper (Naus et al 2003) that refers to.
3. Methods: Where controls used to define positivity (or negativity)? If so what
4. Methods: what is the sensitivity of the parasite counting?
5. methods: why no IgG1?
6. Results: It is unclear from the text whether the suggestion to base the conclusion on school aged children is due to the low numbers of <5's (n=33 for high transmission season, pg 11 2nd para).
7. Discussion: I think the discussion is too long – the first two paragraphs are more back ground than discussion and distract from the data presented
8. The discussion of serological responses needs to be organised better and more circumspect. I find the results presented in the MS acceptable & believable but there context needs to be better presented. The argument switches between using prevalence and magnitude (or levels) of Ig responses to a variety of antigens in a variety of other studies. The inherent problem here, and with which I have some sympathy, is that methodology is not standardised in these different sites. Cut offs used to define positivity are likely to vary widely and be largely endpoint driven. Thus that define clinical endpoints are different to those that are more epidemiologically orientated – I would stick to the latter. Even then the prevalence differences between the cited Gambia and Drakely studies will in some part be due to methodology. The method presented here uses an assay which does not seem to be easy to standardise – the differences between the Burkina faso data and those presented in the MS highlight this. If as the authors suggest mapping a serological reponses can be used in other areas then is it not likely a mass produced recombinant antigen is more likely to provide standardised results between sites over time? The argument that a mixed antigen prep is likely to reach saturation is flawed – there will antibody competition for binding sites and other factors that influence the response, though I agree that simple sero-prevalence is a weak analysis and the approach presented here is more useful.
9. Figures – n or N should b included in the legends as these change depending on whether all or seasons are included

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)
What next?: Accept after minor essential revisions

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

Quality of written English: Acceptable

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

Declaration of competing interests:

I currently hold a grant which is involved in a full evaluation of serological responses to malaria antigens as markers of malaria transmission.