Reviewer's report

**Title:** Comparative Study of Effectiveness of Two Antifolates Prophylactic Strategies against Malaria in HIV Positive Pregnant Women in Bangui, Central African Republic (MACOMBA study protocol): a randomized open label control trial

**Version:** 3  **Date:** 13 May 2013

**Reviewer:** Christine Manyando

**Reviewer's report:**

1. The study design is adequate to test the hypothesis for this study which is very relevant in the light of the ever increasing resistance to SP and the added burden of malaria among HIV infected pregnant women. This design also addresses the information gap related to the outcomes of CTM use in pregnancy in a randomized clinical trial as most reports provided so far on this subject are derived from studies not primarily designed to explore the effects of CTM on malaria in HIV infected women. The antimalarial effects have been documented but not in this vulnerable target population.

2. The details provided in the protocol are sufficient to allow replication of the work or comparison with related analyses.

2.1 However, with regards to participant information (the study population), the last statement ‘Women who already know their HIV status can also be included if their CD4 count is >350 and they have no opportunistic diseases (WHO stage 2, 3 and 4’, there is need to further clarify this statement as to whether the women will be re-tested and CD4 count checked at this stage of inclusion in the study or whether, the previous information shall form basis for recruitment (minor essential revision).

2.2 As regards to the eligibility criteria, the protocol is silent concerning the women who will be found to have malaria parasites (asymptomatic and symptomatic) at recruitment and yet they fulfill all other inclusion criteria, are these women going to be treated before inclusion? Or will they be excluded, treated and later perhaps re-considered for inclusion when they are no longer parasitaemic? -(Major compulsory revision)

2.3 The background information/relevance (rationale) did not reflect the current prevalence of malaria in the study area, to provide the burden of disease among the study population. This information is essential. Additionally, perhaps this information could help clarify whether; there would be a number of potential study participants with parasitaemia or symptomatic malaria at the time of recruitment as indicated in the item 2.2 above. (Major compulsory revision)

2.3 Under recruitment and randomization: perhaps further details on exactly how the randomization is being carried out will make this section clearer. It is
mentioned that randomization will be centralized and stratified according to maternity clinic and gravidity. The actual process of how this will proceed is not entirely clear.(Discretionary revision)

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

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

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.