Reviewer's report

Title: Establishing the extent of malaria transmission and challenges facing pre-elimination in the Republic of Djibouti

Version: 1 Date: 2 March 2011

Reviewer: David Smith

Reviewer's report:

The study described in this manuscript describes the results of a large national parasitological survey recently conducted in Djibouti as part of the National MIS. The report is more than a report on the MIS because it also reports on a serological survey conducted using the filter papers collected at the same time as the rapid diagnostic test. This method (serology) has long held the promise of being able to collect important information about the history of transmission in low intensity settings such as Djibouti. The study found much higher seroprevalence than prevalence.

The study concludes that 1) malaria prevalence is very low in Djibouti today and there is no strong evidence of high rates of malaria importation, so that it would be a place where elimination would likely be technically feasible; 2) that malaria seroprevalence is indeed, highly sensitive. It's very well written and designed and most of what I'm saying here falls into the category of picking at nits.

I confess I had to look up Getis-Ord, but I now understand a new statistical test and it was appropriate for the kind of data that they have. I did wonder whether the hot spots had significant Z-scores for prevalence separately or for seroprevalence separately, (as opposed to and/or) and whether the hot spots were in the same place. It wasn't clear and could be interesting.

One question about the decision "not to use traditional three standard deviations above established control sera but have used a mixture model..." It would be good to know how well this has been validated for malaria markers where serology is trickier than it is for rubella and measles. This seems like it could be quite important, because of the possibility for false positives. It could, on the other hand, lead to much more reliable use of serology. It merits asking whether it has been used and validated for malaria before? It might be worth a more extensive comment one way or the other.

I have a couple of quibbles about language, one or two are minor but essential and worth trusting the authors to make:

Abstract line 3: "these are of less value" less than what? I suspect they mean to say that they are unlikely to find any positives and so they convey little information about malaria transmission, even with very large and expensive surveys. I think the right term is "not very efficient"
Results last line: "increasing combined P. falciparum exposure" I'm not sure the word combined belongs there.

Bottom of page 3: "has low sensitivity" Again, a quibble, but they don’t mean sensitivity, which in this context, could be confused with the idea that there may be lots of low density infections that tend to be not detected when present by a single test (see their ref 27), but the fact that at very low endemicity, they are bound to find lots of true negatives and very few positives. Again, I would opt for "efficient" over some other term.

Top of page 4: "define the extent of transmission" seroprevalence is telling you something about the history of transmission, not necessarily about current transmission. Add the word "previous"?

Page 5, 2/3 down: "anticipated over-distribution" I think they mean "over-dispersion"

Page 6, near the top: "The estimated required sample was..." required for what? Later, the text mentions net usage, but it would be worth mentioning that fact here. Also, what effect size was it powered to detect?

Page 12: "A unit increase..." Do age groups have units? I'm not sure what they mean. "A one age-group increase"?

Page 14 near the top, there's an errant "[" or it was not closed.

Page 15 "the significance of human population movement for the risks of imported infectious diseases, including malaria, cannot be under-estimated" Do they really mean that? Or do they mean that they should not be under-estimated. Of course it's possible to under-estimate the risks.

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

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

It is an easily ascertainable fact that I have published with AMN, RWS, and CJD. Even so, none of those connections rise to the level of a conflict.

I declare that I have no competing interests.