Reviewer’s report

Title: Determining the efficacy of guppies and pyriproxyfen (Sumilarv® 2MR) combined with community engagement on dengue vectors in Cambodia: study protocol for a randomized controlled trial

Version: 0 Date: 10 Feb 2017

Reviewer: Thomas Smith

Reviewer’s report:
Basic information on the scale of the trial should be evident in the abstract (i.e. number of clusters, sampling effort).

The statement of what is the primary outcome should mention how the mosquitoes are trapped (both in the summary and on p12 under 'Primary Outcome Measure'. From the rest of the paper I understand this to be adult resting collections, as described on p15.

The introduction sections provide a very thorough review of the evidence on Aedes interventions in Cambodia, but very little data from elsewhere. It would be good to see more detail on the global evidence base for the interventions being tested, while the information on interventions that are not being tested could be made more concise.

P4 line 22: the description of PPF as an intervention needs to specify how this is deployed. Clearly the impact of any larviciding intervention is conditional on the coverage and the frequency of deployment.

P6 line 16: one hopes that the trial will 'test' or 'estimate' the community effectiveness of the interventions. 'Demonstration' of the effectiveness would assume that the result is already known.

P6 line 18: hypothesis 1 should be explicit that the hypothesis relates to the combination of interventions (not the interventions separately).

P7 line 9: there is a broken link to a reference.

P7 line 13 et seq.: how were cluster sizes and boundaries determined? The number of clusters is rather small, and the study would presumably be more powerful with more, smaller clusters.

P7 line 20: how do the authors know that a 200m buffer will be sufficient to avoid spill-over effects? If the mosquitoes fly an average of 50-100m per generation, then one might anticipate spill-over effects over longer distances with multiple generations of mosquitoes. How will the investigators know whether such effects happen or not? Will the data all be geolocated, allowing investigation of edge effects?
P8 & p9: The omission of a guppy only, or COMBI only arm appears to mean that the incremental impact of the guppies will not be identifiable. This could lead to a package of interventions being promoted, that includes a significant useless component. How will the investigators determine whether any effect is accounted for by COMBI, or guppies, or if both are required?

P12: the list of secondary outcome measures includes measures of adherence or coverage as well as of intervention effect. It would be helpful to see some indication of which fit into each category; it would also be helpful to see the rationale for each outcome measure, and how these data will be analysed.

P14 line 13. Has the allocation already been carried out, or is it still to take place? The statement about putting sheets of paper on the wall is in the past tense.

P18. The statistical methods section is rudimentary. It is not clear what comparative measures between the arms will be calculated. Presumably effectiveness will be estimated as proportionate reductions, relative to the control arm. How will confidence intervals and significance tests be carried out? How will the statistical analysis allow for clustering? Will there be any attempt to use process measures derived from the secondary outcomes to attribute causality?

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