**Reviewer’s report**

**Title:** Lactoferrin and Lysozyme to Reduce Environmental Enteric Dysfunction and Stunting in Malawian Children: Study Protocol for a Randomized Controlled Trial

**Version:** 0  **Date:** 07 Sep 2017

**Reviewer:** Stephen Allen

**Reviewer's report:**

This is a valuable protocol but, as below, more information about the study needs to be provided as directed by the SPIRIT guidelines.

The last sentence of Abstract: "Effective" should be removed from "these safe and effective proteins" - as this will not be known until the results are available.

Page 4, line 8: Clarify the statement that "Infants who never breastfed are 14 times likely to die from all causes" was shown in studies done in low and middle-income countries.

Page 4, line 13; Should "Specific to children with minimal dietary diversity" be "Similar to children…"?

Page 4, line 32: state what "expressed significantly elevated levels of the anti-inflammatory cytokine TGF-β1"

Page 6, lines 38-53: The primary outcome should be specified more clearly. Is the "decrease of 0.06 units in L:M" the difference in the means for each arm - and over what time period (8 or 16 weeks)? Other outcomes (e.g. absorption of individual sugars) should be secondary outcomes.

Page 6, line 55: Similarly, state how linear and ponderal growth will be calculated and over what time period.

Page 8: provide more details re who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions.

Page 9, lines 4-10; what quality assurance measures will be done to ensure accurate measurements (e.g. weighing children independently twice and comparing findings)?

Will the use of antibiotics (which would likely impact on gut microbiome and possibly effectiveness of the interventions) be monitored during the trial?
The following additional information is needed according to SPIRIT guidelines:

* How will adherence with the interventions be evaluated?

* Has a DMEC been established? If not, justification needed. What are the arrangements for collecting and reporting adverse events?

* Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial

* State plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct

* Who will obtain informed consent or assent from potential trial participants?

* How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial

* Statement of who will have access to the final trial dataset

* Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions

* Authorship eligibility guidelines and any intended use of professional writers

* Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code

* Add model consent form and other related documentation given to participants and authorised surrogates as an appendix

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