Reviewer's report

Title: Experimental infection of healthy volunteers with enterotoxigenic Escherichia coli wild-type strain TW10598 in a hospital ward

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Reviewer: Carlton Gyles

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General comments:
This is a well written report in which the authors provide valuable background information and a sound rationale for evaluation of a new strain of enterotoxigenic E. coli (ETEC) with respect to safety and dose response in human experimental infection. The objectives of the research are clearly stated and the research constitutes an important contribution to the literature on human challenge studies with ETEC. The study demonstrated the safety and effectiveness of the challenge protocol with ETEC strain TW10598 and identified a dose that is optimal for studies of vaccine efficacy. The title and abstract accurately reflect the study and its findings.

The study, involving 30 volunteers in a hospital in Norway, took a little over 2 years, with 1 or 2 patients being challenged at a time and the authors acknowledged that a dedicated unit would be needed to carry out a phase IIIB vaccine trial.

Discretionary revisions:
1. The methods are appropriate but there is a question regarding the detection of the challenge organism in stool samples. The authors used PCR and a melting curve analysis to detect STh and LT-A genes as markers of the ETEC challenge strain TW10598 and stool specimens were considered positive for this strain if the PCR detected the STh and/or the LT-A genes. The authors may wish to indicate why detection of only 1 of the 2 marker genes was acceptable as an indicator of the presence of the challenge ETEC strain.

2. The diarrheal responses to the target dose of 109 CFU appeared to be similar with respect to attack rate but less severe than that to the 108 CFU dose as indicated by severity, mean incubation period, 24 hours maximum stool output, whole episode stool output, mean episode duration, and 24 hours maximum stool output count (Table 1). The authors may wish to comment on these findings.

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

Quality of written English: Acceptable
**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests.