Letter to the Editor

Ensuring access to oral cholera vaccine to those who need them most

Dear Editor,

Saha and colleagues report results from a vaccine trial in Bangladesh showing high thermal-stability of Shanchol [1]. These results are highly encouraging for the large scale use of killed oral cholera vaccines (OCV) in places where maintaining cold chain can be highly challenging, and where OCV might have its greatest impact. We would like to comment on two additional issues not deeply discussed in the manuscript that are critical to translate this research into public health benefit.

First, the schemes tested in this study likely do not represent the upper limit in terms of heat-stability of Shanchol. Another study with a similar killed OCV exposed to 42 °C for six months showed that potency was preserved (measured in terms of lipopolysaccharide content) and that the vaccine retained immunogenicity in a rabbit model [2]. This suggests that the upper limit for heat and duration of exposure while retaining potency remains unknown. In fact, it is possible that a cold chain is not required at all for Shanchol. This represents not only a critical regulatory and economic question, but also an ethical issue. Maintenance of the cold chain is more challenging in remote rural areas, and it is in these areas where cholera causes the most devastating consequences [3]. Thus, many additional individuals among those at highest risk of dying from cholera could benefit from killed OCVs at a lower overall cost if the vaccines could be stored and used outside of the cold chain.

Nonetheless, it seems unlikely that a regulated out of cold chain use of Shanchol will be established in the short term; thus, consideration is needed regarding the vaccine vial monitor (VVM) for this vaccine and its use in control temperature chain (CTC). The available VVMs indicate thermal-stability at 37 °C at different intervals (2, 7, 14 and 30 day intervals). Currently, Shanchol vaccine has a VVM 14, which means that stability is guaranteed when exposed at 37 °C up to 14 days. Data from the study conducted by Saha et al. clearly suggest that vaccine is stable at 42 °C for 14 days, but does not determine if it remains stable for a longer interval. The lack of concordance between the available VVMs and the conditions used in this trial pose a barrier to fully capitalize the findings of this study, which could potentially include constrains for flexible CTC conditions. So far, the only vaccine prequalified with CTC specifications is MenAfriVac, which is labeled to be use at 40 °C for a maximum of 4 days under controlled temperature.

The results from Saha et al. clearly indicate that CTC conditions could be extended for Shanchol and the lack of adapted VVMs should not be a barrier for more flexible CTC conditions. As soon as the CTC use for OCVs is established, pilot projects should be conducted during a campaign before the standard protocols are adopted in order to optimize OCVs use in CTC with field based insights [4].

In our opinion, additional potency studies testing longer intervals at higher temperatures are needed along with new VVM developments and CTC piloting allowing for more flexible use of thermal-stable vaccines. The World Health Organization through the prequalification process is already working with the two manufacturers that provide vaccines to the global vaccine stockpile to obtain additional stability data at high temperatures. Eventually, the ideal development would be to establish a regulated out of the cold chain use of OCVs if stability can be proved in such conditions. This development would increase access of OCV for those who need it most. In addition to changing the way that OCVs is used, this will reduce implementation costs and will increase the impact of OCV in controlling cholera worldwide.

References


Francisco J. Luquero *
Anne Ballard
David A. Sack

DOVE Project, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, United States

* Corresponding author.

E-mail address: fluquero@epicentre.msf.org (F.J. Luquero)