

SUPPLEMENT 1: Rationale underlying the AMR monitoring strategy

The GTFCC recommends that any studies of antibiotic chemoprophylaxis for cholera requires evidence that considers the emergence of antibiotic resistance.¹ Doxycycline has been frequently used for seasonal (mass) malaria chemoprophylaxis in Africa, and resulting increased levels of resistance among parasites have not been documented in current studies at clinically-relevant levels.² Doxycycline's impact on extended-spectrum beta-lactamases (ESBL) producing *Enterobacteriaceae* is considered negligible as compared to azithromycin. For mass chemoprophylaxis with azithromycin for trachoma and prevention of child mortality, transient increases in AMR among *Enterobacteriaceae* were detected.^{3,4} Therefore, if antibiotic chemoprophylaxis with azithromycin is used in CATI, a nested cohort study of AMR will be undertaken. A description of presence of AMR at baseline and post-administration (in *Enterobacteriae*) will be performed among persons receiving antibiotics in a subset of rings. In addition, if doxycycline or azithromycin are used, routine systematic AMR monitoring in *V. cholerae* isolates will be undertaken.⁵ Given concerns of rapidly-increasing resistance specific to ciprofloxacin, we do not recommend its use for selective chemoprophylaxis.^{1,6}

References

1. Global Task Force on Cholera Control (Case Management Working Group). Interim Technical Note: Use of antibiotics for the treatment and control of cholera Geneva, Switzerland: WHO,; 2018 [Available from: http://www.who.int/cholera/task_force/use-of-antibiotics-for-the-treatment-of-cholera.pdf?ua=1].
2. Schechner V, Temkin E, Harbarth S, et al. Epidemiological interpretation of studies examining the effect of antibiotic usage on resistance. *Clin Microbiol Rev* 2013;26(2):289-307. doi: 10.1128/CMR.00001-13
3. Keenan JD, Arzika AM, Maliki R, et al. Longer-Term Assessment of Azithromycin for Reducing Childhood Mortality in Africa. *N Engl J Med* 2019;380(23):2207-14. doi: 10.1056/NEJMoa1817213
4. Doan T, Arzika AM, Hinterwirth A, et al. Macrolide Resistance in MORDOR I - A Cluster-Randomized Trial in Niger. *N Engl J Med* 2019;380(23):2271-73. doi: 10.1056/NEJMc1901535
5. Global Task Force for Cholera Control. Antimicrobial Susceptibility Testing for Treatment and Control of Cholera 2021 [Available from: <https://www.gtfcc.org/wp-content/uploads/2021/04/gtfcc-job-aid-antimicrobial-susceptibility-testing-for-treatment-and-control-of-cholera.pdf>].
6. Mashe T, Domman D, Tarupiwa A, et al. Highly Resistant Cholera Outbreak Strain in Zimbabwe. *N Engl J Med* 2020;383(7):687-89. doi: 10.1056/NEJMc2004773 [published Online First: 2020/08/14]