

Introduction

In principle, all people at risk of cholera should receive an oral cholera vaccine (OCV).¹ The killed whole-cell (WC) vaccine, Shanchol, available through the global stockpile, is safe, easy to administer, relatively inexpensive and effective. If a high proportion of the population is vaccinated, herd protection will greatly enhance its effectiveness.² When OCV programs are integrated with improved water and sanitation and quality health care, no one should die from cholera. Theoretically, cholera can be eliminated as a public health problem from many countries where it is now endemic with a comprehensive package of interventions.

What ethical issues could there be with regard to cholera vaccination? In principle, OCV should simply be provided to all persons at risk. However, as with any new intervention, questions about the ethical use of the vaccine have been raised and will continue to be raised as its use expands. This brief document identifies some of these questions and provides guidance concerning ethical issues that may arise when considering the use of OCV.

IRB reviews

When will review by an ethical review committee (or institutional review board, (IRB)) be needed before a vaccine campaign is started? An IRB review is only required prior to using the vaccine for research purposes. Since Shanchol and Euvichol have been pre-qualified by the World Health Organization and were shown to be safe and effective, administration of these vaccines should be similar to that of other vaccines

¹ There are currently three WHO prequalified, killed whole cell oral cholera vaccines, Dukoral, Shanchol, and Euvichol. Shanchol and Euvichol are the vaccines available through the global stockpile. See [Oral Cholera Vaccine: What You Need to Know](#) for a description of the vaccines.

² Herd protection means that in a community with many vaccinated individuals; even those who did not receive the vaccine will have a lower risk because the transmission of the infectious agent is reduced.

provided through the public sector. The Expanded Program on Immunizations (EPI) routinely provides vaccines to children. Other vaccines are administered during emergencies. Such routine and emergency vaccines are provided for public health use, and there is no need for a specific ethical committee review. Their safety and efficacy have been well demonstrated in clinical trials prior to their licensure and WHO pre-qualification.

Will an evaluation of a cholera vaccination campaign require an ethical review? Generally, if the agency or the Ministry of Health wishes to evaluate a vaccination campaign to improve program effectiveness or efficiency, this will not require a review by an ethical committee.

On the other hand, if the evaluation involves “human subject’s research,” in which information from individual subjects is recorded and analyzed with the intent to publish scientific papers, the study protocol needs to be reviewed by the appropriate ethical review committee(s) before initiating data collection. Informed consent from individuals may also be necessary, depending on the situation.

A research project which requires IRB approval should not however, delay implementation of a public health program which is already proven to be effective and needed to control a cholera emergency. When attempting to control a cholera emergency, protecting the health of the people through the vaccination program should take priority over the research project.

Equity: who will be offered the vaccine?

Since the vaccine supply is limited, what principles of equity determine who will receive the vaccine?

The global supply of OCV is limited and there are 69 countries with endemic cholera. There is no way, at present, to provide the vaccine to everyone who may be at risk. Thus, the vaccine needs to be allocated to population groups in a manner that it is equitable.

When a country does obtain the vaccine, how does it determine which groups should receive vaccine

and which should not? These are difficult questions and local officials will have to conduct an analysis to determine how best to use the vaccine which is available. Depending on the local epidemiology and context, local officials should consider issues of equity when making these choices.

Possible options include vaccinating geographic areas considered to have the highest rates such that the vaccine can avert the most numbers of cases. Another option is to target people living in remote areas where there is limited access to health care where the risk of dying of cholera is highest.

If the goal of OCV campaigns is to save the most lives, this suggests that vaccine campaigns should indeed be targeted to persons living in remote areas who are at the highest risk of death. However vaccinating persons in these remote areas may also be more expensive and are logistically more difficult. It may not be feasible to get vaccine to these groups. These choices are not easily made.

Ethics of “off label” use

Is it ever ethical to use only a single dose of Shanchol rather than the two doses as recommended? Shanchol is registered as a two-dose vaccine and this is not likely to change soon. However, there is new evidence that a single dose does provide some protection. This protection, although less than two doses, may result in a greater population benefit in certain situations. For example, giving a single dose provides vaccine for twice as many people as two doses and may, in fact, prevent more cases. A recent paper provides greater detail on single-dose options³ and effectiveness studies are now being reported showing a single dose to provide at least short term protection.^{4,5}

If the single-dose strategy is to be used, policy makers must understand its risks and benefits. The program might also consider a second dose later on, when it

³ Azman AS, Luquero FJ, Ciglenecki I, Grais RF, Sack DA, Lessler J (2015) The Impact of a One-Dose versus Two-Dose Oral Cholera Vaccine Regimen in Outbreak Settings: A Modeling Study. *PLoS Med* 12(8): e1001867. doi:10.1371/journal.pmed.1001867.

⁴ Azman AS, Parker LA, Rumunu J, Tadesse F, Grandesso F, Deng LL, et al. Effectiveness of one dose of oral cholera vaccine in response to an outbreak: a case-cohort study. *The Lancet Global health*. 2016;4(11):e856-e63

⁵ Qadri F, Wierzbza TF, Ali M, Chowdhury F, Khan AI, Saha A, et al. Efficacy of a Single-Dose, Inactivated Oral Cholera Vaccine in Bangladesh. *N Engl J Med*. 2016;374(18):1723-32.

becomes feasible to do so, and this may help address equity issues.

Cold chain issues. The label directs the vaccine to be kept cold. However, the major protective antigen in the vaccine (lipopolysaccharide) is heat stable, and there is evidence that the vaccine is stable when stored at ambient temperature for several weeks. The opportunity to distribute vaccine without a strict cold chain lowers costs and simplifies logistics of the campaign, potentially making vaccine available to vulnerable groups who may not receive it if the cold chain must be strictly maintained.

Before adopting this strategy, the global health community should consider whether there are ethical issues in using a vaccine in a manner that is not in accordance with the label, and should determine what additional evidence is needed for national and local policy makers to consider this option.

OCV and pregnancy

Should OCV be given to pregnant women? Because OCV is a killed vaccine that is taken by mouth, there is no rational basis for suspecting that OCV is unsafe for a pregnant woman or her fetus.

The World Health Organization recommends the vaccine be given during pregnancy because the benefits of vaccine outweigh any risks for persons for whom vaccine is being given.

For more discussion about the use of OCV during pregnancy, see [Cholera and the Use of Oral Cholera Vaccines in Pregnant Women](#).

Conclusions

This is only a start toward identifying the potential ethical questions that will arise as OCV becomes more widely used. The DOVE project is developing a full paper on this topic and, in preparation, would appreciate your questions and suggestions. Please feel free to contact the DOVE project at www.stopcholera.org with your thoughts.