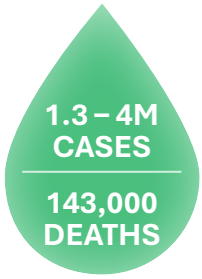
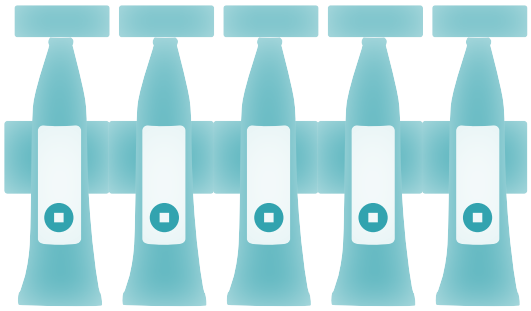
Controlled Temperature Chain

Simplifying the delivery of oral cholera vaccine

BACKGROUND

Cholera poses a significant public health threat, especially in areas with poor sanitation and limited access to clean water. An estimated 1.3 to 4.0 million cases occur each year, resulting in up to 143,000 deaths across the globe.[1] Although cholera is both preventable and treatable, its incidence has increased since 2021. Ongoing conflicts, climate change, natural disasters, and limited access to safe water, sanitation, and hygiene have contributed to the wider geographic spread of the disease and rising numbers of cases, deaths, and case fatality rates.





Oral cholera vaccines (OCVs) are an effective, proven solution for reducing the risk of cholera infection. Currently, three OCVs are prequalified by the World Health Organization (WHO). Traditionally, these vaccines must be transported and stored within a standard 2°C to 8°C cold chain. This requirement can pose logistical challenges for rapidly delivering cholera vaccines and reaching last-mile communities in low-resource settings.

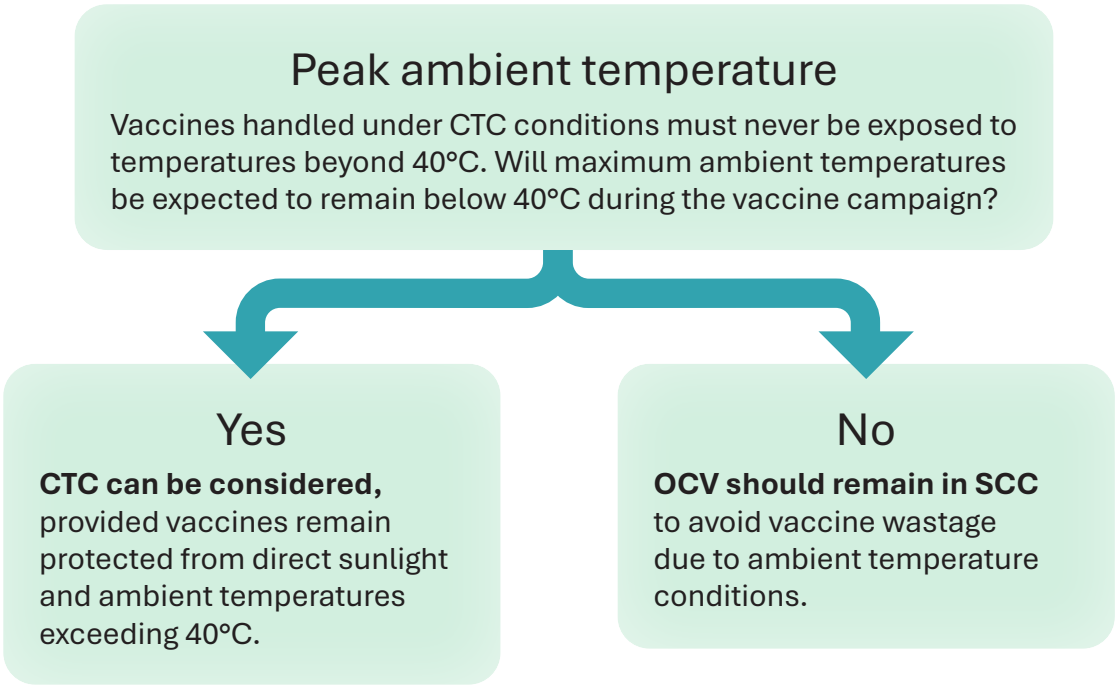
The controlled temperature chain (CTC) is a WHO-endorsed vaccine management strategy that allows certain vaccines to be kept at temperatures outside of the standard cold chain (2°C to 8°C) under specified conditions. Each vaccine approved for CTC has a maximum allowed number of days it can be kept at these temperatures. Currently, there are three WHO pre-qualified oral cholera vaccines currently available (Dukoral®, Euvichol-Plus®, and Euvichol-S®). Euvichol-S® is expected to receive WHO qualification in 2026 for use in CTC.

World Health Organization

PATH

Controlled Temperature Chain for Oral Cholera Vaccine

Operational considerations for applying CTC in an OCV campaign: A key objective of CTC is to equip vaccine campaign leaders and vaccinators with an additional, complementary approach to overcome burdens and constraints associated with delivering vaccines in a standard cold chain (SCC). Several considerations should be taken into account when assessing the potential use and impact of CTC in OCV campaigns. These include the following:



Additional factors to consider

Campaign duration: Vaccine campaigns expected to last a shorter duration than a vaccine's approved CTC period can easily implement CTC strategies. Campaigns expected to last longer than the approved CTC period will require careful management, including the staged removal of vaccines from cold storage and careful tracking of the CTC expiry date to ensure the quality of all doses administered.

Reach: In settings where vaccine campaigns face challenges accessing remote, isolated populations, CTC approaches can help overcome logistical, operational, and geographic barriers by simplifying campaign activities (e.g., eliminating the need for ice packs, reducing daily resupply trips, and lowering weight carried by health staff). Reaching remote communities with in situ vaccination can help build trust and rapport with the health system.

Vaccine staging: Cold chain infrastructure can vary across and within countries. CTC approaches complement standard cold chain practices, providing vaccine campaign managers with a proven and flexible management strategy in locations where cold chain infrastructure is limited or nonfunctional. CTC can be initiated in various levels of a health system and adapted to different campaign strategies.

Vaccine safety: CTC eliminates the risk of freezing, as no ice packs are used. In addition, lack of humidity and condensation in vaccine carriers without ice packs reduces the risk of damage to vaccine labels, a common cause of wastage during campaigns and outreach.

Key implementation steps for OCV campaigns using CTC

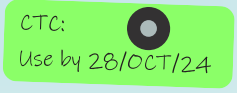
Applying CTC requires several actions by national-level and district/health facility staff.

Key CTC materials

Campaign leaders will use target population totals and expected OCV vaccine presentation to estimate and purchase two critical CTC supplies:

1) Peak temperature threshold indicators (PTTIs) that are color-changing, adhesive stickers indicating when heat exposures surpass 40°C.

2) Green expiry stickers that indicate an end of CTC period.



CTC monitoring and reporting

CTC monitoring tools can help generate campaign insights and analyses.

Preparations and procurement

Procure CTC materials (PTTI indicators [LIMITmarker® I-K or VVM-TI, color adhesive labels).

Campaign site planning

Incorporate CTC into microplans. Estimate target populations and determine how many vials to remove from the cold chain to minimize vaccine wastage.

Training

Orient national and district health staff and volunteers on CTC handling and monitoring. Attach PTTI and CTC expiry dates on vaccine secondary packages. Define CTC implementation and adapt CTC training and monitoring materials.

Vaccination

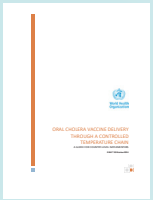
Vaccinators verify PTTIs, vaccine vial monitors, and CTC expiry dates and record key monitoring data. Withdraw additional stock from cold chain as needed.

Documentation

Analyze compliance, training, and results and adjust CTC practices for future campaigns.

Implementation materials

The OCV CTC implementation guide and job aid provide national and district vaccine leaders with practical guidance on operationalizing CTC in vaccine campaigns.



Training materials

The OCV CTC training facilitation guide, modules, and scenarios can be used to build capacity of vaccine managers and vaccinators on CTC approaches.

Tools, guides, and modules available upon request from innovation@path.org.

Practical application and lessons learned

CTC for OCV has been implemented in several countries, including Guinea, Malawi, South Sudan, Cameroon, Bangladesh, Mozambique, and Zambia.[2–7] Results from these implementations showed positive feedback from health care workers and demonstrated that CTC can be used safely and compliantly, resulting in efficiency gains and improved vaccination coverage.[8] In Malawi and Zambia, the use of CTC in OCV campaigns contributed to coverage benefits in reaching areas with lack of cold chain capacity, lowering transport costs and freezing risk, and resulting in time savings.[9] Below are key lessons learned and practical approaches for applying CTC practices for OCV campaigns in low- and middle-income countries.

LESSON LEARNED #1

CTC approach achieves higher vaccination rates in Zambia

Key lessons:

1. **Simplified operational logistics:** CTC eliminates the need for daily vaccine resupply trips that are required in an SCC to maintain cold temperatures, lowering costs and transportation requirements.
2. **Expanded reach:** The elimination of ice packs, time and labor for conditioning ice packs, and weight/volume of ice packs reduces preparation time and enables vaccination teams to transport more vaccines each day.

In 2020–2021 Zambia's Ministry of Health, with WHO and other organizations, implemented an OCV campaign in the high-risk rural districts of Nsama and Shibuyunji. The campaign served as a randomized study to compare the total number of individuals vaccinated using SCC approaches compared to CTC approaches.

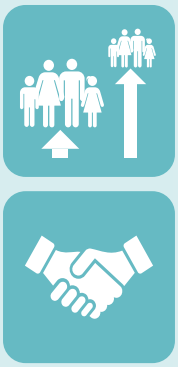
Barriers in these districts included a limited or absent cold chain at smaller facilities, long distances, difficult terrain, periodic flooding, and unreliable energy supply. These challenges made daily vaccine resupply difficult. The study included 59 vaccination teams using CTC and 61 using SCC conducting two rounds of vaccination that reached 262,711 individuals.

At the end of the study, more people received OCV through CTC (53.2 percent) compared to SCC (46.8 percent). This was achieved despite a higher OCV wastage rate for CTC (635 vials vs. 4 vials for SCC). The primary cause of the CTC wastage was the inadvertent exposure of vaccines to temperatures over the 40°C threshold in an area where sugar cane fires were burning. Overall, 90 percent of the CTC team members indicated a preference for use of CTC in future campaigns, citing its simplified workflow and logistics.

LESSON LEARNED #2

CTC strengthens community trust in health programs in Mozambique

Key lessons:



1. **CTC expands equitable reach:** By removing cold chain constraints, CTC eases logistics in remote and crisis-affected areas, ensuring last-mile communities do not miss out on vaccination.
2. **CTC strengthens community trust:** By allowing vaccination teams to reach remote communities, CTC enables direct, in-person outreach under CTC conditions, which fosters dialogue, dispels misinformation, and demonstrates the health system's commitment to reaching last-mile households.

Building and maintaining community trust—particularly for last-mile households—is essential for the success of vaccination campaigns and public health interventions. Families in remote or underserved areas often face significant barriers accessing health services due to a variety of factors, ranging from geographic and structural gaps (topography, extreme weather events, and infrastructure) to health system limitations (human resources, operational constraints, funding). These barriers can reinforce a sense of neglect and weaken confidence in the health system. CTC approaches offer immunization teams a practical solution for addressing this divide by enabling health workers to bring vaccines directly to hard-to-reach populations while creating opportunities for meaningful, trust-building engagement.

In 2019, Cyclone Idai—one of the most powerful and deadliest tropical cyclones to affect African countries—struck Mozambique and severely damaged the health and cold chain infrastructure. Flooding and the damaged water and sanitation infrastructure contributed to the onset of a cholera outbreak. The Mozambique Ministry of Health quickly responded by launching an emergency cholera vaccine campaign in four target districts. CTC practices were integrated into the vaccination campaign microplans in areas where the cold chain was no longer present.

CTC approaches helped the Ministry of Health and campaign staff achieve two major goals: 800,000 OCVs were delivered, and health workers strengthened trust within communities. CTC approaches enabled campaign staff to expand the reach of campaign activities to remote and underserved areas by reducing time and energy required to prepare and transport ice packs, reducing the weight of vaccine carriers, and reducing overall operational budgets. In-person outreach and transparent dialogue allowed vaccinators to directly engage with families, address misconceptions with OCV, and demonstrate the health system's commitment to last-mile communities. Ultimately, by demonstrating commitment and respect, health care workers using CTC approaches can contribute to building lasting relationships with communities and the health system, laying the foundation for future health interventions and stronger, more resilient immunization programs.

LESSON LEARNED #3

Adaptive strategies for managing CTC supplies and heat exposure in Bangladesh

Key lessons:

1. **Flexible and adaptive approaches for CTC logistics:** Differences in OCV packaging and dose presentation may require creative approaches to PTTI management.
2. **Harness local problem-solving capacity:** Locally-derived, creative solutions can limit potential heat exposure risks during vaccine campaigns.
3. **Accurate forecasting and monitoring to reduce CTC expiration date wastage:** Careful planning is needed to ensure vaccines removed from the cold chain are used during the CTC period.

In January 2025, Bangladesh's Cholera Program launched a large-scale reactive OCV campaign in Cox's Bazar and Bandarban districts, reaching more than 1.4 million people using CTC practices. Campaign managers were confronted with several challenges, including a shortage of PTTIs and heat exposure risks during vaccine transport and staging. Creative, adaptive measures demonstrate how practical innovation and rapid learning can sustain vaccine integrity in CTC.

Campaign managers planned to place one PTTI on each vaccine package, assuming 50-dose packaging. However, the arrival of 10-dose packages resulted in a significant PTTI shortage. Teams began reusing PTTIs on empty vaccine packaging as temperature-monitoring cards—an adaptive solution that enabled continual ambient temperature monitoring.

Of the 25,257 OCV doses discarded early in the campaign, 36% (8,852) were reportedly exposed to temperaturese above 40°C as indicated by black PTTIs. Investigation showed that heat from exposure to direct sunlight and hot surfaces—even with moderate 26° to 28°C ambient temperatures—was causing temperature excursions. Although vaccine carriers and cold boxes without ice provide protection against warm temperatures, vaccination teams used alternative equipment that was easier to carry and required the following practical heat-reduction measures:

- **Sunlight protection:** Teams were instructed to keep vaccines shaded with umbrellas, transport them during cooler hours, and avoid midday exposure.
- **Transport adaptations:** Vaccines were repacked in insulated bags or protective boxes, trucks were modified to allow airflow beneath vaccine containers, and black tarps were replaced with white reflective covers.
- **Distribution point relocation:** Storage and staging areas were moved from open spaces to shaded or enclosed structures to minimize radiant heat exposure.

Finally, the loss of 15,719 doses (discarded due to those vaccines reaching their ten-day CTC expiration date) highlights the need for carefully planning the vaccine quantities brought into CTC against the remaining target vaccination goal.

Ultimately, the Bangladesh campaign demonstrated that with proactive heat mitigation and strong coordination, CTC can deliver potent, validated vaccines safely and effectively to communities in challenging conditions.

References

1. World Health Organization. Cholera. Geneva: WHO; 5 Dec 2024. https://www.who.int/news-room/fact-sheets/detail/cholera

2. Grandesso F, Rafael F, Chipeta S, et al. Oral cholera vaccination in hard-to-reach communities, Lake Chilwa, Malawi. *Bulletin of the World Health Organizatio*n. 2018;96(12):817–825. https://doi.org/10.2471/BLT.17.206417

3. Khan AI, Islam MS, Islam MT, et al. Oral cholera vaccination strategy: self-administration of the second dose in urban Dhaka, Bangladesh. *Vaccine*. 2019;37(6):827–832. https://doi.org/10.1016/j.vaccine.2018.12.048

4. World Health Organization (WHO). After tropical cyclone Idai Sofala Province successfully conducts second round of oral cholera vaccination. WHO; July 24, 2019. https://staging.afro.who.int/news/after-tropical-cyclone-idai-sofala-province-successfully-conducts-second-round-oral-cholera

5. Kapaya F. Performance of vaccination campaign using oral cholera vaccine with & without control-temperature chain, Zambia, 2021. Global Task Force on Cholera Control; December 8, 2021. https://www.gtfcc.org/wp-content/uploads/2022/01/8th-meeting-of-the-gtfcc-working-group-on-ocv-2021-day-3-fred-kapaya.pdf

6. Porta MI, Lenglet A, de Weerdt S, et al. Feasibility of a preventive mass vaccination campaign with two doses of oral cholera vaccine during a humanitarian emergency in South Sudan. *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 2014;108(12):810–815. https://doi.org/10.1093/trstmh/tru153

7. Ciglenecki I, Sakoba K, Luquero FJ, et al. Feasibility of mass vaccination campaign with oral cholera vaccines in response to an outbreak in Guinea. *PLOS Medicine*. 2013;10(9):e1001512.

8. CTC Realist Review: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9306389/pdf/BLT.21.287696.pdf

9. MoH interview on 2016 Malawi campaign; VIPS Dalberg CTC Independent Assessment