4 The Market Shaping Goal

Ensure healthy markets for vaccines and related products

Gavi Alliance MS Roadmap for

Oral Cholera Vaccines

Public Summary

Purpose and scope

The roadmap is a foundational tool of Gavi's market shaping strategy with the purpose to articulate a mid- and long-term market strategy designed to align market-shaping objectives and target outcomes across the Alliance partners, define a set of interventions to reach these objectives and target outcomes, and inform procurement strategies and decisions. The objectives, target outcomes and interventions articulated in this roadmap focus on provision of oral cholera vaccines (OCVs) for Gavi supported countries, while including global market considerations to highlight interdependencies and their impact on overall market health.

Current epidemiological context of Cholera and Gavi engagement

Cholera is an acute diarrheal infection caused by ingestion of food or water contaminated with the bacterium *Vibrio cholerae.* Each year there are an estimated 1.3 to 4.0 million cholera cases and 29,000 to 143,000 deaths worldwide[1]. Today cholera affects approximately 50 countries across the globe and approximately 80 million people are living in cholera hotspots in Africa alone[2]. The disease occurs as an endemic disease in some areas and can persist or reappear regularly in hotspots in geographically limited areas, causing major outbreaks; it also regularly occurs in the context of humanitarian emergencies where there is limited access to clean water and improved sanitation. Cholera control measures include improvements in water, sanitation and hygiene (WASH), vaccination, timely detection of and response to outbreaks, and appropriate case management. The primary route to long-term control and elimination of cholera will be through WASH interventions. However, the Oral Cholera Vaccine (OCV), which has a duration of protection of approximately 3 years, is important to control the spread of disease in areas prone to disease transmission, and bridge between emergency response and longer-term cholera control measures. The 2017 position paper by WHO advised that OCVs should be delivered through mass vaccination campaigns and used in areas with endemic cholera, in humanitarian crises with high risk of cholera, and during cholera outbreaks. The paper also states that vaccines should always be used in conjunction with other cholera prevention and control measures as part of a comprehensive cholera control strategy.

The Global Task Force on Cholera Control (GTFCC) is a global network of organizations involved in the fight against cholera across all sectors; it's secretariat is located at the World Health Organization (WHO). In October 2017, GTFCC issued a call to action through a new strategy *'Ending Cholera, a Global Roadmap to 2030'* which calls on countries, technical partners and donors to step up their efforts and pool their resources to reduce cholera deaths by 90% and eliminate cholera in up to 20 countries using a multi-sectoral cholera control strategy, including the use of OCV in targeted areas. In 2013, the WHO established an OCV emergency stockpile to be able to deliver vaccines quickly in outbreak situations, which is managed by the International Coordinating Group (ICG[3]) and is supported by Gavi. In 2018, Gavi's Board expanded support for planned, preventive OCV use in "hotspot" geographies, while continuing Gavi's stockpile support for emergency response needs. Since January 2023, Gavi integrated the preventive OCV programme within its portfolio , meaning countries are able to apply for multi-year campaign support through routine Gavi processes and are encouraged to include activities related to cholera control in other Gavi funding grants. This transition to longer term preventive campaign planning is expected to expand the preventative programme and integrate Cholera vaccination campaigns into the wider immunisation landscape, which is expected to improve visibility and predictability of preventative demand.

Demand for OCV has been steadily increasing since the first vaccine suitable for Gavi markets received WHO prequalification. In a supply constrained environment, doses are prioritised for emergency response over preventative campaigns. From 2017 to 2021, approximately half of available doses were able to be allocated for preventive use, after all emergency vaccine needs were met. However in 2022, a surge in cholera

[1] Ali M, Nelson AR, Lopez AL & Sack DA. Updated Global Burden of Cholera in Endemic Countries. PLoS Negl Trop Dis 2015,9(6)
[2] Ending Cholera, A Global Roadmap to 2030, The World Health Organization, 2017
[3] The ICG is composed of four Alliance partners: the International Federation of Red Cross and Red Crescent Societies (IFRC), Médecins Sans Frontières (MSF), UNICEF and WHO

worldwide resulted in very few doses being available for preventative use and substantial unmet preventive demand.

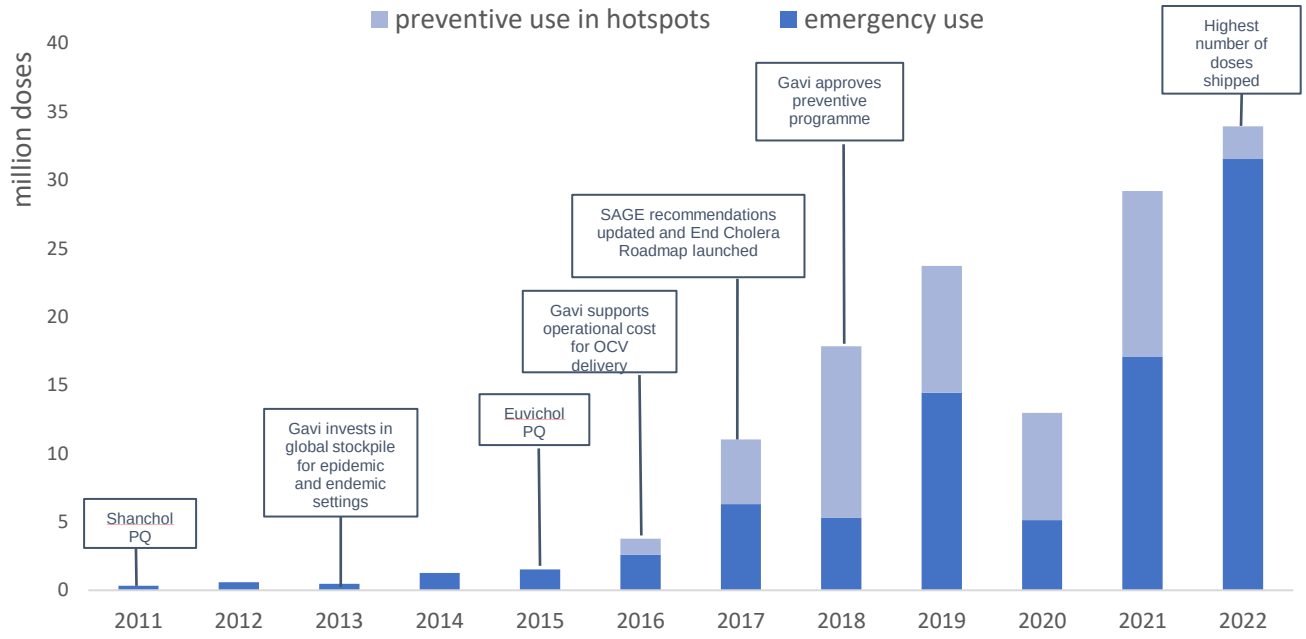


Figure 1: historical supply of OCV 2011-2022

Market health and evolution

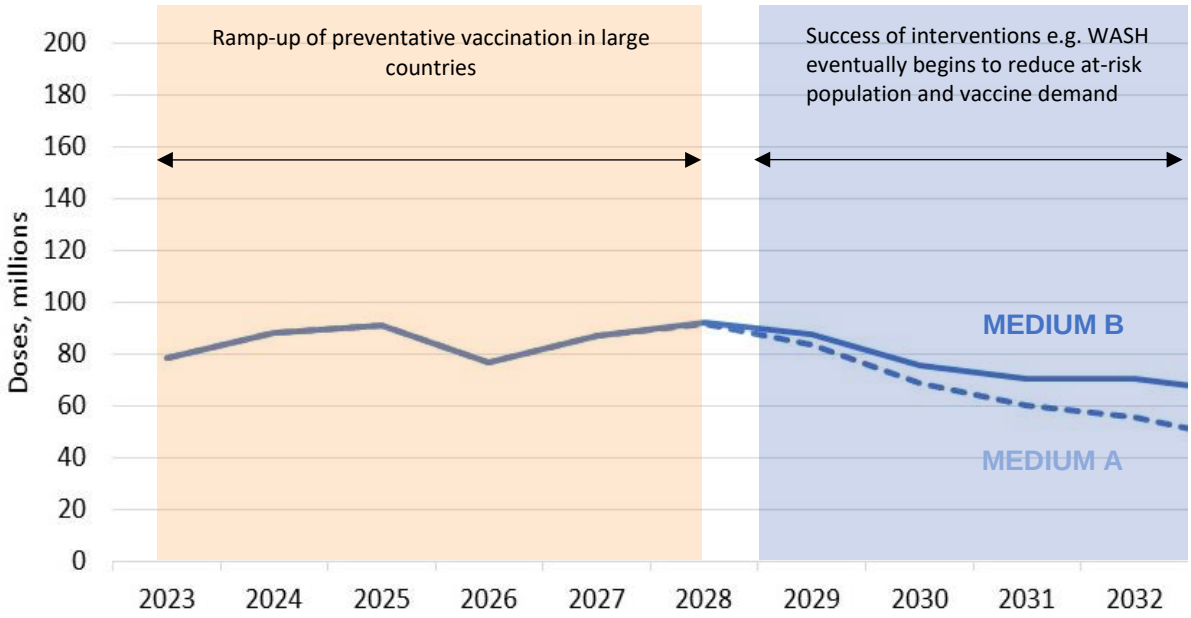
Figure 2 shows two scenarios that estimate demand for OCVs in the absence of supply constraints for both the preventative programme and emergency response, combined. With the launch of the Gavi preventative programme in 2023, countries are encouraged to begin planning multi-year preventative campaigns, and implementation will commence soon thereafter, as supply allows. Average demand in these scenarios is approximately 85M (million) doses annually between 2023 and 2030, excluding India. In a high demand scenario, annual volume needs could be up to 220M doses annually[4]. This variability in demand is driven by, scope and timing of country launches, frequency of revaccination, variability in target populations for preventative campaigns and uncertainty in emergency response needs. Medium A and medium B scenarios show moderate and conservative decreases in demand post-2030 respectively following completion of initial preventative campaigns resulting in a reduction in at risk populations. Medium A is aligned with the End Cholera Roadmap and assumes a continuous decline in at risk populations following high investment in WASH programmes and infrastructure, and large-scale implementation of OCV campaigns in the previous period. Medium B reflects a scenario where there is a slower decrease in at risk populations maintaining a high need for OCV due to multiple factors including slower roll out of improved WASH infrastructure and programmes, and other cholera-control programs, and potential changes in transmission dynamics.

Currently, two manufacturers supply a WHO prequalified OCV programmatically suitable for Gavi countries: Sanofi Healthcare, India previously known as Shantha (producer of Shanchol) and EuBiologics (producer of Euvichol and Euvichol Plus), South Korea. Sanofi supplied 100% of Gavi demand until 2016, and since its launch in 2017, EuBiologics has supplied more than 70% of Gavi needs. Sanofi will exit the market at the end of 2023 and has been supplying low annual volumes (<5 million doses) since 2020. There are multiple

[4] Not shown in figure, for more information on OCV demand forecasting, contact forecasting@gavi.org

additional licensed oral cholera vaccines serving small-scale markets (including travellers)[5] and there are at least three additional developers of pipeline candidates expected to achieve licensure before 2030 including: Bharat Biotech International Limited (BBIL), India and Biovac, South Africa and BIBCOL, India.

Figure 2: Strategic demand scenarios for OCV *in the absence of supply constraints* for Gavi supported countries, October 2022



Healthy market dynamics and challenges over the next 10-years

OCV 'market health' is categorized as **unacceptable and requires further intervention** given that all high and medium impact 'healthy market attributes' are either unmet or only partially met. Market health is expected to improve in the medium term to acceptable levels but is unlikely to be sustainable without significant risks until 2030.

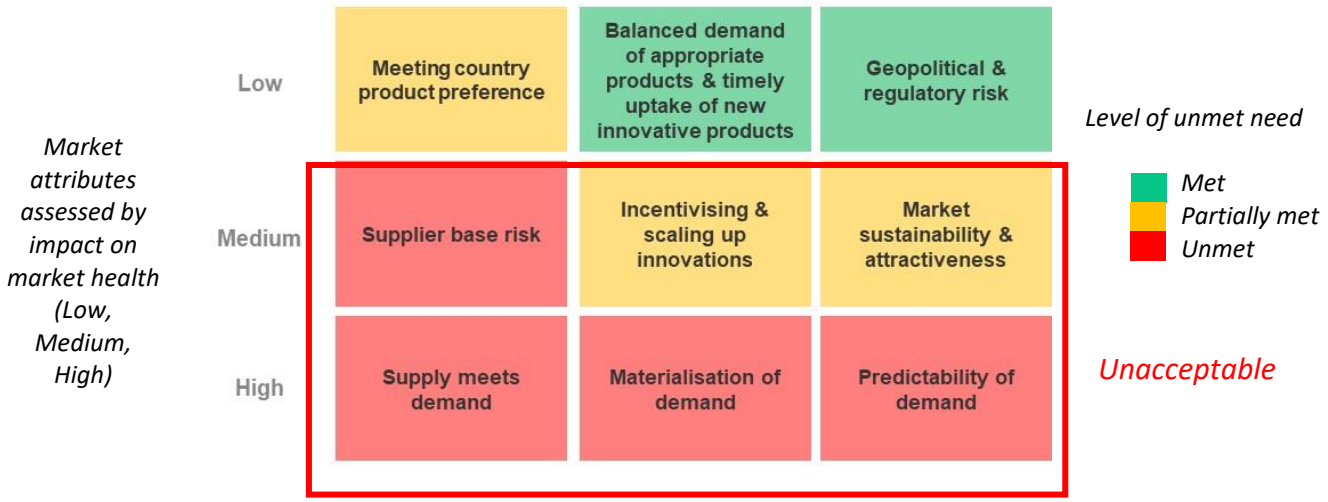


Figure 2: OCV Market Health Assessment 2022, based on Gavi Alliance Healthy Market Framework

[5] These include but are not limited to mORCVAX from Vabiotech, Vietnam, Cholvax from Incepta Vaccine Ltd, Bangaldesh, Vaxchora from Emergent Biosolutions, USA, Dukoral from Valneva, Sweden, and Oravacs from Shanghai United Cell Biotechnology, China.

The OCV market shaping roadmap covers a period of 9 years (2023 – 2031), which can be divided into three phases, based on supply and demand dynamics.

Phase 1 short term: (2023 – 2025): The supply constraint currently affecting the OCV market is expected to continue until approximately 2025. During this time the doses will be allocated between all needs (emergency response and preventative campaigns) according to stockpile guidelines and preventative use allocation principles due to be published soon. Sanofi will exit the market at the end of 2023 (although they have been supplying only 10-15% of annual volumes since 2020) and the remaining incumbent, EuBiologics cannot support the full anticipated demand in this period, although supply availability will increase starting in 2024 thanks to investments in production capacity expansion. Another manufacturer is expected to enter the market increasing supply and reducing supplier base risk towards the end of this period. During and beyond this period of constrained supply, it will be critical to maintain countries' momentum to develop and implement comprehensive long-term national cholera prevention and control plans, including the targeted use of OCV in hotspots.

Phase 2 medium term (2026 – 2030): Supply is expected to increase and begin to meet both emergency and preventive demand at the start of this period. Supply capacity increases are expected, and a third manufacturer may enter the market. If expected capacity increases are realised, delayed preventive campaigns from Phase 1 will be able to be completed and demand predictability will improve. This will likely be an intense period of phased preventive campaigns across large countries assuming programme momentum can be sustained through the supply constrained period. It is also anticipated that India may begin a Cholera vaccination programme during this time, possibly affecting supply of OCV to Gavi supported countries. Locally licensed OCVs may become important.

Phase 3 longer term (2031+): Market dynamics post 2030 will be determined in large part by progress made in phase 2 (preventative campaign and supply scale-up success), and more importantly WASH program implementation in relation to the level of ongoing need for vaccination of new or persistent at-risk populations. It is hoped product innovations such as improved temperature stability, longer duration of protection, and improved effectiveness in children will have proved their additional benefits and potentially advanced to market from this time point onwards.

Strategy to sustainably improve market health

Gavi Partners defined a long-term strategy for the cholera vaccine market to address these challenges, which translates into the following strategic market objectives and target outcomes, and corresponding interventions.

Objective 1: Supply is optimized in the short-term, meets demand in the mid-term, and a secure and sustainable supplier base exists over the long-term

Supply is anticipated to increase in both the short and medium term, however Alliance actions could accelerate these increases and further secure supply for the long term.

- Target Outcome 1: In the short-term (2023-25), sustainably 'maximise' supplier production output
- Target Outcome 2: By mid-term (2026) and beyond, supply meets demand as estimated in figure 2
- Target Outcome 3: At least 2 suppliers sustainably supply UNICEF over the long-term

A concerted action plan ensures the coordination between Gavi market shaping partners and facilitates the achievement of the above strategic market outcomes. Actions include the following:

- Explore and implement strategies to accelerate market entry, at scale, of at least one new supplier, and support the incumbent supplier to maximise supply availability.

- Develop and apply an allocation framework for preventive campaigns in order to ensure equitable and transparent access to OCV, and provide consistency in demand
- Improve forecasting: stabilize short-term demand forecast to enable improved production planning, and build confidence in long-term forecast to provide clear market signals for pipeline developers
- Review existing guidance on OCV use for emergency response to ensure timely and appropriate OCV use while maintaining momentum of preventive campaign implementation
- Refresh understanding of demand outlook post 2030 and supply sustainability requirements

Objective 2: Improve materialization, predictability and quality of preventative OCV programme

The recent high volume of doses and proportion of global supply needed for emergency response has made it difficult to plan for and deliver preventative campaigns, and the limited supply available for preventive campaigns may discourage countries from planning future preventive campaigns. As well as challenging programmatically, this volatile emergency-based demand can be unattractive to suppliers and a barrier to increased supply. Success in a preventative cholera programme, while of course reliant on assured increased supply, will support further supply scale-up through improved demand predictability. Progress will be especially important in the short-term to ensure the engagement currently seen by countries is maintained.

➢ Target Outcome 4: In the short term (2023-2025) optimise preventative demand materialisation, stabilizing the demand forecast and maintain programme momentum: preventative campaigns and minimum supply needs are predictable for a three-year horizon with an annual country-specific allocation as a result of timely and high-quality country planning and multi-year applications.

Related interventions:

- Increase accuracy and trust in long term supply availability for preventive campaigns through communicating regularly within the Alliance, and to countries and extended partners.
- Review vaccine funding guidelines for preventative programmes, monitor implementation for appropriate use of OCV within long-term cholera control strategy, and review accordingly.
- Support quality country applications and long-term planning processes:
  - Proactive communication on strategies for OCV use and support available from the Alliance
  - Disseminate guidance on best practice hotspot mapping to allow best practice demand characterization and allocation of limited supply that maintains country momentum
  - Explore additional resources and technical guidance to support countries' preventative programme applications and high-quality campaign implementation
  - Ensure countries have comprehensive risk assessments and multi-year vaccination plans, improved surveillance using diagnostics, , and political will to submit applications
  - Update guidance to countries for reactive campaign planning, including humanitarian settings, and to ensure quality reactive campaign applications and implementation and adequate bridging with OCV preventive use

➢ Target Outcome 5: In the mid to long term (2026+) demand predictability moves beyond three-year time horizon as preventative approach entrenches, and cholera vaccination is reflected in national immunisation strategies and 5-year routine immunisation planning cycles in countries with endemic cholera

Related interventions

- Support countries to coordinate and integrate cholera vaccination plans with other national public health plans (e.g. through national Cholera control plan and National Immunization Strategy (NIS)).
- Develop guidance and collect data to routinely monitor programmatic indicators on quality and timing of multi-year preventative campaigns
- Develop and disseminate policy and guidance on revaccination in endemic hotspots
- Continue evaluating the appropriate size of the emergency stockpile supported by analysis

Objective 3: Innovations are identified, and research priorities are accelerated including longer lasting protection and higher protection in children, and a pathway to WHO prequalification is established

Many cholera vaccine candidates are in development but there is a lack of guidance and coordination from programmatic partners on what innovations should be prioritized (with the exception of labelling updates below), and what demand for specific product profiles may be.

- **Target Outcome 6**: Controlled Temperate Chain (CTC) included in labelling for all new products by 2025
- **Target Outcome: 7**: Value and use case of innovations is understood and signalled to manufacturers, including high and long-lasting protection in children and adults, and pathway to WHO prequalification is established.

Interventions:

- Ensure new and existing products provide information on vaccine safety for pregnant women
- Identify use cases and establish protocols for CTC
- Ensure comparators exist to allow WHO prequalification of future innovations
- Develop a white paper on the value and use case of cholera vaccine product innovations in the Gavi market