The Market Shaping Goal

Shape vaccine markets to ensure adequate supply of appropriate, quality vaccines at low and sustainable prices for developing countries.

Supply and Procurement Roadmap

Cholera Vaccine

Public Summary
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Cholera affects the poorest and most vulnerable populations around the world, it is closely associated with poor sanitation and lack of clean drinking water, and causes approximately 2.9 million cases per year that result in approximately 95 thousand deaths.

The Global Task Force on Cholera Control (GTFCC), a global network of organisations involved in the fight against cholera across all sectors, issued a call to action ‘Ending Cholera, a Global Roadmap to 2030’ in 2017, with an overall objective “to reduce the mortality resulting from cholera by 90% by 2030, and to eliminate cholera in as many as 20 countries”. Its strategy includes the use of vaccines in emergency settings (outbreaks and humanitarian situations) and in campaigns targeted to cholera hotspots, as part of a multisectoral strategy that includes WaSH interventions (Water, Sanitation and Hygiene).

- WHO’s Strategic Advisory Group of Experts (SAGE) defined in August 2017 its position on the use of oral cholera vaccines that includes pre-emptive campaigns.
- The World Health Assembly in May 2018 issued resolution WHA71.4 that supports implementation of the GTFC roadmap to 2030.

A global OCV stockpile is in place since 2013; it includes volumes for use in emergency situations managed by the International Coordinating Group (ICG) and volumes for use in endemic areas managed by the GTFCC oral cholera vaccine (OCV) Working Group.

Gavi has been engaged in cholera vaccination since 2014 through the funding and support of the global stockpile of cholera vaccines. The 2018 Gavi Vaccine Investment Strategy (VIS) for the period 2021-2025 recommended cholera as an investment for campaigns among high-risk populations in sub-national hotspots in addition to the stockpile for emergencies and was conditionally approved by the Gavi Board in November 2018. If confirmed by the Gavi Board in June 2019, the investment will change the nature of Gavi’s commitment to fighting cholera by shifting it from a support to emergency epidemic outbreak control to a long-term support of the integrated and global control of cholera as a disease in endemic countries.

This roadmap is based on the assumption that the VIS exercise concludes with a final decision by the Gavi Board to invest as described above. This is necessary because of the urgent need to support market dynamics through implementation in 2019/2020 of the appropriate market shaping and procurement strategies. A review of the roadmap will take place immediately after the outcome of the VIS in June 2019 to integrate the Gavi Board’s final decisions and their implications if not already accounted for.

As currently modelled, the cholera vaccination strategy could avert 21 to 660 thousand deaths and 2 to 26 million cases between 2025 and 2035 at a procurement cost of USD 1 to 1.9 billion.

Market overview

Demand

Gavi demand for OCV increased from approximately 0.2 million doses (md) in 2013 to over 13md in 2017. The travellers and military market is estimated at about 1.3md/year.

In line with the epidemiology, Gavi considers 39 Gavi-supported countries that are target for cholera control; they are referred to in this document as Gavi39 and include: Afghanistan, Angola,
Bangladesh, Benin, Burkina Faso, Burundi, Cameroon, Chad, Congo DR, Congo Rep., Cote d’Ivoire, Djibouti, Eritrea, Ethiopia, Ghana, Guinea, Guinea-Bissau, Haiti, Kenya, Liberia, Malawi, Mali, Mozambique, Myanmar, Nepal, Niger, Nigeria, Pakistan, PNG, Sierra Leone, Somalia, Sudan, South Sudan, Tanzania, Togo, Uganda, Yemen, Zambia, Zimbabwe. The roadmap focuses on these countries that are considered at highest risk for cholera, and on India.

The stockpile use of OCVs for outbreak response is expected to remain around 5md between 2019 and 2023 and to stabilize at 2.5md from 2028.

The OCV volume required for endemic use in Gavi39 countries is expected to increase to approximately 18md in 2018, 31md in 2019, 64md in 2021, reaching approximately 74md in 2022, and may stabilize at about 65-70md from 2025-2026. Bangladesh is expected to represent on average 36% of the Gavi39 demand during 2018-2028.

In addition to Gavi39, the demand for India (not Gavi-supported) is unknown and will depend on the country’s future strategy to contain cholera. If OCV become a core part of India’s plans and its target population is the size that is currently estimated, demand for India could reach up to 20md within 3 years and 80md between within 6 years.

Beyond Gavi39 and India, other countries may require up to 4.3md in 2019, 12md in 2023, and 7md in 2028. The travellers and military market is expected to increase from about 1.3md to 2md/year over the next ten years.

Estimated historical & potential future market volume (mid-point scenario) (million doses).

Sensitivity on demand:
Currently, there is a range of plausible demand scenarios due to the relatively recent scale up of the programme, to multiple interacting factors, and to the nature of the disease management. This range will reduce in the mid-term, as more countries implement well-planned campaigns and WaSH interventions that are successful and sustainable. However there will likely be some degree of residual volatility long-term, in particular related to humanitarian crises and to renewed OCV demand in areas where WaSH related investments/infrastructures are insufficiently well maintained.
Supply landscape
Currently, two manufacturers supply a WHO pre-qualified OCV suitable for Gavi countries: Shantha (Shanchol) and Eubiologics (Euvichol and Euvichol Plus). Both manufacturers are expected to increase supply capacity over the period 2019-2022.

Incepta of Bangladesh is developing Cholvax, an OCV that may be locally licensed in 2020. A further two to three new prequalified OCVs that are programmatically suitable for Gavi countries may be available between 2020 and 2023.

Overall, supply available to Gavi may increase from approx. 20md in 2018 to over 40md in 2020, 60md in 2022, reaching 100md in 2024 and over 110md from 2025.

Balance of supply and demand
Supply for Gavi38 countries (Gavi39 excluding Bangladesh) is expected to be below demand during the period 2019-2022, to narrowly meet demand in 2023-2024, and may have some limited buffer capacity from 2025. In 2025-2028, buffer capacity available to UNICEF-SD beyond Gavi-supported demand will be dependent on progress towards controlling cholera; it may be that demand reduces and buffer capacity increases linked to a decrease in preventive campaigns due to successful and widespread WaSH programmes (this would potentially create availabilities elsewhere such as for India or Bangladesh if these countries are not yet self-sufficient), or it may be that programmes are less successful than anticipated and demand for OCV vaccination increases.

Bangladesh may start covering large volumes as soon as Incepta’s OCV is available for procurement on behalf of Gavi. Its supply may start in 2021 but is expected to be -53% below demand on average until 2025 and may approach demand in 2027-2028.

India demand is expected to be covered by local manufacturers and supply is likely to be short of India’s demand for the next 10 years.

Price
The UNICEF weighted average price (WAP) remained stable at USD 1.85 between 2013 and 2015; it decreased by 3% to USD 1.79 in 2016, and to USD 1.77 in 2017. It is expected to reduce by a further 20 to 25% in 2018. Gavi prices are 4-5% of prices in private markets.

Market Value
The global market for cholera vaccines is expected to reach approximately USD 110 million in 2019, over USD 260 million by 2022 and USD 300 million by 2028.

Healthy Market Framework Evaluation
The Cholera market is in a low level of health from 2018 to 2022, evolving towards moderate during the period 2023-2024, and possibly high from 2025. The low rating in 2018-2022 is linked to the unconstrained demand required for full implementation of the GTFCC ‘Roadmap to 2030’ increasing faster than the expected increase of supply.

Currently, the cholera market only meets one of the eight market attributes (NRA risk), partly meets 4 attributes (meet country preferences, individual supplier risk, product innovation, long term competition) and meets the buffer capacity requirement.
innovation, total system effectiveness), the supply meets demand attribute is rated between partially met and met (see explanations below), and the cholera market does not meet two attributes (buffer capacity, long term competition).

Supply meets demand: Partially met / Unmet. Following the fast increase in manufacturing capacity 2016-2018, supply has allowed to start the vaccination program of the GTFCC ‘Roadmap to 2030’ and to broadly meet the WHO demand forecast for Gavi39 in 2018. However, this 2018 demand forecast is partly supply-constrained and the timing of available doses is regularly not in line with the timing of some campaigns resulting in temporary unmet demand. From 2019, supply will not meet the ideal unconstrained demand. At the same time however, it is unclear whether countries will have the capacity to operationally implement introductions as they communicated to the GTFCC. This complex and evolving situation leads to rate this market attribute as between partially met and met for 2018. This complex and evolving situation leads to rate this market attribute between partially met and met.

Country presentation preference: Partially met. Countries currently accept any available vaccine.

Buffer capacity: Unmet. Buffer capacity is expected to be available only from 2023, reaching 10% of Gavi39 demand from 2024 which may still be insufficient.

Individual supplier risk: Partially met. Both current manufacturers have recently shown good reliability on supply forecasts and capacity increase but performance at significantly higher capacity is untested.

NRA risk: Met. NRA risk is low with current manufacturers.

Long-term competition: Unmet. One manufacturer is expected to provide approximately 70% of Gavi supply excluding Bangladesh 2018-2022. However, there is a pipeline of 4 new cholera vaccines with some potentially becoming available 2018-2023.

Product innovation: Partially met. Current OCVs satisfy the minimal requirements for achieving GTFCC goals but have 3 shortcomings: only 3 years of protection, less efficacious in young children, 2 doses required.

Total systems effectiveness: Partially met. Current OCVs are convenient orally administered vaccines available at reasonably affordable prices. However, the need to re-vaccinate after 3 years reduces systems effectiveness and increases costs considerably.

Overall:

Short- to mid-term, the most critical market shaping issue for cholera control is to improve the predictability of future demand while ensuring the required supply.

Long-term, the most critical market shaping issue for cholera is to improve the duration of protection; it will increase the long-term effectiveness of vaccine interventions, reduce the drain on resources, and increase cost-effectiveness.
Supply and Procurement Objectives

Supply and procurement objectives were analysed resulting in the following target outcomes:

- Manufacturers supply to Gavi≥48 md by 2021 and ≥84 md by 2023, including specific targets for supply to Bangladesh by 2021 and 2023.
  - The Bangladesh NRA is assessed to be ML3 (functional) by 2021 or an alternative NRA release solution is set up.
  - One new manufacturer supplies Gavi from 2021 and at least one additional manufacturer by 2023.
- Mitigation strategies that address the risk of potential under-supply or of challenges to sustainability are in place by end 2019; decisions are reviewed every year.
- New vaccine candidates that target over 10-years protection and improved child immunogenicity are in clinical development by 2023.
- By 2022, two or more improved presentations (plastic tube, tablet, other country preferences) are available, all vaccines supplied to Gavi have a registered CTC option, and a 1-dose schedule is registered or under regulatory review.
- The UNICEF-SD WAP/dose reaches its target value (confidential) for 2020 and for 2024.

Gavi’s future market shaping exit conditions: Gavi will stop its market shaping efforts when supply meets demand in a diverse and sustainably healthy market and when cholera control is on track to achieve the GTFCC’s objectives of the roadmap to 2030 and vaccination volumes are reducing. This is unlikely to occur before the period 2030-2035.

Supporting Stakeholder Action Plan

A concerted action plan ensures the coordination between Gavi Alliance stakeholders; it is designed to facilitate the achievement of the above supply and procurement target outcomes.

- UNICEF-SD’s next procurement process for OCV will take place in 2020 for supply in 2021 and beyond.
- Develop the operational factors that will help improve demand dynamics and the related forecast reliability:
  - Plan in detail and with countries the operational implementation of the GTFCC and VIS-derived cholera control strategy; prepare country applications, plan campaigns, set priorities, and prepare contingency plans; by the end of 2019 ensure that demand forecasts are rooted into detailed country plans as guided by the above; partners (GTFCC, Gavi, BMGF) define a clear process for tracking demand and create a list of indicators that link to demand predictability by the end of 2019; continuously monitor the evolution of the cholera situation in India including epidemiology, NITAG discussions, and health policy.
- Encourage/support manufacturers to increase supply capacity. Identify potential market shaping activities that contribute to such an evolution. During the period 2019-2022, track annually progress of demand and supply and adapt market shaping activities accordingly.
- Encourage/support pipeline manufacturers to develop candidate OCVs that are appropriate for the Gavi market.
- Provide solutions to support the effective development of Bangladesh’s NRA towards sustainable functionality or alternative solutions.
- Define the Gavi-country target presentation profile(s) that meet operational needs and engage manufacturers to develop optimized presentations that meet the above target.
- Define the desired long-term target product profile(s) that would provide major improvements over existing OCVs in the context of cholera control and engage manufacturers to develop such vaccines.