

# 4

## The Market Shaping Goal

*Shape markets for vaccines and other immunisation products to achieve moderate or high levels of healthy markets dynamics.*

---

### Supply and Procurement Roadmap

# *Typhoid Conjugate Vaccine (TCV)*

[Public Summary](#)

## Public Summary

Improvements in living conditions and the introduction of antibiotics have largely eliminated typhoid in industrialised countries, however typhoid continues to affect populations without access to safe water, improved sanitation and safe food, and is a public health concern for many people in Gavi supported countries. The emergence and spread of antimicrobial resistant strains of *Salmonella Typhi* is another growing cause for concern. The WHO recommends programmatic use of typhoid vaccines for the control of typhoid fever, with a preference for typhoid conjugate vaccine in view of its improved immunological properties, suitability for use in younger children and expected longer duration of protection.

The Gavi Board prioritised TCVs as part of the 2008 Vaccine Investment Strategy (VIS) with the expectation that an appropriate vaccine would obtain WHO prequalification (PQ) by 2011. A number of factors caused delays in vaccine development and it was only in November 2017 that the Gavi Board approved the opening of a funding window for TCV, in light of SAGE recommendations on the use of TCVs and the upcoming prequalification of a Vi-TT vaccine.

Gavi now provides support for the introduction of TCV into the routine immunisation schedule and a catch-up campaign of up to 15 years of age. Depending on epidemiology, countries may choose to introduce the vaccine sub-nationally or only focus on routine introduction. The Gavi Board also approved the use of TCV in outbreak response, but with a decision not to create a stockpile given limited knowledge on the use of the vaccine in outbreak situations and the importance of not diverting supply away from preventive / routine vaccination.

A number of factors will determine when active market shaping support by Gavi might end, including sufficient and sustainable quality assured long-term supply from a diverse base of suppliers, affordability of prices to ensure continued vaccination programmes, and WHO position on typhoid vaccination in the context of improvements in water and sanitation.

## Market Overview

Demand for TCV will be built from scratch with the opening of Gavi's funding window, but a number of factors will contribute to uncertain country uptake: lack of disease burden estimates, potential future improvements in water and sanitation, competing immunisation priorities, and less Gavi support and fiscal space in the context of increasing Gavi transitions.

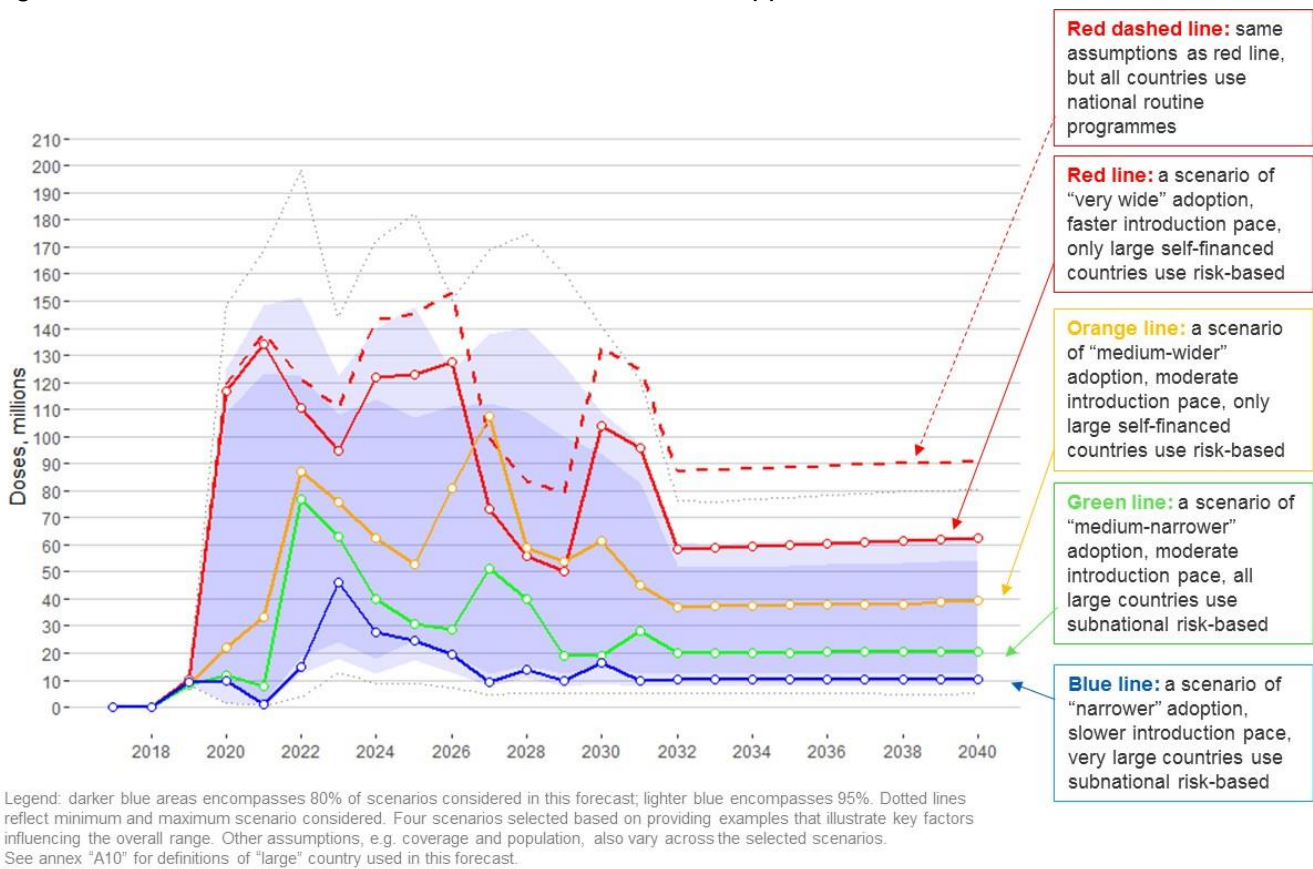
It is anticipated that countries, particularly those in Africa, will require targeted activities (e.g. generation of better burden of disease data, cost effectiveness analyses or co-administration studies) to make informed decisions regarding TCV introduction into routine immunisation schedules.

Another driver of uncertainty in future demand is country's choice to pursue national vs. risk-based sub-national immunisation programmes. WHO primary recommendation is routine immunisation leaving ample room for varying implementation of catch-up campaigns.

In the absence of confirmed country plans, Gavi TCV demand forecast for Gavi 73 supported countries (see Figure 1) exhibits a wide range of scenarios and high variability of demand on a year-to-year basis reflecting demand peaks from large catch-up campaigns in the year of introduction. The higher scenarios illustrate demand potentially peaking at above 150 million doses in 2022, with a period of several years where demand could be well over 100 million doses per year, stabilizing later at levels above 60 million doses per year. The lower scenarios illustrate the potential for demand to stabilize around 10 million doses per year in the long-term, with a shorter term period where volumes would likely be above this level as campaigns are conducted.

In the absence of good surveillance data and considering population migrations, it is worth drawing attention to another risk-based approach which assumes that all countries will conduct national routine immunisation. For the high demand scenario, the resulting long-term demand would be 90 million doses per year, above the highest levels illustrated in the ranges of the current forecast.

Figure 1: TCV Demand Forecast March 2018 – 73 Gavi-supported countries



It is worth noting that renewed country engagement since the opening of the Gavi funding window has resulted in newly available information on country plans and there are indications that several countries could apply for TCV introduction over 2018 and 2019. As country plans formalize, in terms of introduction timing and scope, the demand forecast will need to be updated.

In an environment with only one prequalified vaccine, the scale of supply available in the next few years will be highly dependent on that manufacturer capacity and the timely market entry of new manufacturers. The currently prequalified vaccine is recommended for single dose routine vaccination, and available in multi-dose vials.

When considering very high demand scenarios, forecasted supply will be unable to meet demand levels for several years. When considering very low adoption and demand scenarios, forecast supply should be sufficient to meet demand. In more moderate adoption scenarios, the balance between demand and supply could vary based on a number of factors. The engagement with manufacturers on the nature and timing of key decision points, as well as the dialogue with large countries, will be particularly important as swings between supply excesses and supply constraints could be dependent on the decisions of just a couple of countries or a single manufacturer. Catch-up campaigns for example will need to be planned carefully over the next several years to ensure that their timing, size and pace are manageable in light of available supply.

### Healthy Markets Framework Evaluation

Considering the uncertainties on the direction of demand in the next few years, the TCV market is expected to have low levels of healthy market dynamics in the near term, partially meeting six of the Healthy Market Framework attributes (highlighted in yellow), while two attributes remain unmet.

The greatest risk to manage for this market is the uncertainty of demand and the implications on supply availability. As the range of demand scenarios starts narrowing, supply needs will become clearer.

Supply Meets Demand: **Partially met**. This attribute depends on the shape of demand, as well as supply dynamics in the context of a newly prequalified TCV and the current early stage of most development programmes.

Country presentation preference: **Partially met**. Depending on supply availability, country product preferences may not be accommodated. In addition, supply availability is initially limited to the 5-dose presentation.

Buffer capacity: **Partially met**. Depending on demand and supply availability, the market may have sufficient buffer capacity or be unable to address unexpected shortages and meet increased demand linked to large catch-up campaigns.

Individual supplier risk: **Unmet**. In the early years of TCV uptake, the market will rely on a single supplier until pipeline manufacturers come to market.

National Regulatory Authority (NRA) risk: **Partially met**. NRA risk is medium with reliance on a single Indian manufacturer and NRA. New entrants should contribute to NRA diversity.

Long-term competition: **Partially met**. Long term competition looks promising considering the rich pipeline of manufacturers, however development progress and timelines will need to be closely monitored. Demand generation and engagement with manufacturers to build confidence in the demand outlook will be critical to facilitate product entries.

Product innovation: **Partially met**. The absence of clearly established country preferences and uncertainties around country uptake limit incentives for product innovation. As TCV programmes scale-up, need for product innovation will need to be re-assessed.

Total system effectiveness (TSE): **Unmet**. Minimal information about country preferences and reliance on a single product and presentation in early years of the TCV programme uptake prevents TSE assessment.

Total System Effectiveness	Long Term Competition	Product Innovation
Buffer Capacity	Individual Supplier Risk	NRA Risk
Meet Country Preferences		
Supply Meets Demand		
Inadequate Supply		

## Supply and Procurement Objectives and Target Outcomes

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

### 1<sup>st</sup> Objective: Balance of MR supply and demand

- Improve predictability of demand in terms of choice of immunisation strategy, schedule, geographical scope and other important variables
- Ensure supply availability to UNICEF from single supplier over 2019-2022 to allow for TCV introductions while managing country expectations
- Reduce single-supplier dependency by ensuring at least two manufacturers offer prequalified vaccines to UNICEF by 2023
- UNICEF supply from at least two NRAs by 2023
- Ensure supply availability and security once market volumes reduce to routine demand only after 2030

### 2<sup>nd</sup> Objective: Cost of vaccine to Gavi and countries

- Achieve price at less than *target value (confidential)* in a 5-dose vial by 2022

- Reduce WAP to less than *target value (confidential)* once supply landscape is more diverse in 2023

**3<sup>rd</sup> Objective: Appropriate and innovative vaccines**

- Establish role of improved TCV characteristics based on programmatic evidence and potential for investment after 2025

**Supporting Stakeholder Action Plan**

An action plan ensures the coordination between Gavi, the Vaccine Alliance stakeholders and is designed to facilitate the achievement of the above supply and procurement target outcomes. The action plan includes the following items:

- Leverage Alliance partners and TyVAC to support countries to assess data requirements for decision making, selection of vaccination strategy, applications, introduction planning, and sustainability
- Narrow the range of the demand forecast and ensure buy-in through timely communication with manufacturers
- If necessary, manage demand and country expectations by scheduling and pacing catch-up campaigns in a manner that allows scale-up in line with supply availability
- Monitor the use of TCV in outbreak response and adjust engagement with manufacturers for outbreak response to minimise disruption to supply allocation as needed
- Support one or more pipeline manufacturers to obtain WHO prequalification for TCV depending on the shape of demand
- Engage manufacturers to understand production economics and impact on supply, and decision making timeline to sustain a diverse supplier base in the market over the long-term
- Engage existing and pipeline manufacturers to ensure Gavi Alliance price targets are achieved
- Review evidence based studies to understand the value of various product innovations and relay back to manufacturers to guide improvement in product characteristics