

Annex C: Investment Framework

Dimension	Description	Typhoid Conjugate Vaccines
Strategic rationale	Trigger for investment proposal	<ul style="list-style-type: none"> In 2008 VIS, the Board prioritised TCVs with other vaccines. June 2017's meeting informed the Board that the Secretariat would update analyses and propose a funding window if TCV was WHO recommended and PQed by the end of 2017. Both are anticipated before the end of 2017.
	Fit with Gavi strategic goals	<ul style="list-style-type: none"> Estimates of 145,000 to 223,000 deaths per year and 11 million to 22 million cases per year, burden has been persistent in Gavi countries while industrialised nations have eliminated this disease 27% of typhoid fever cases in < 5 years of age Aligns to Gavi's mission as well as strategic goals 1 and 4
	Fit with Gavi comparative advantage	<ul style="list-style-type: none"> Significant opportunity to shape the market Currently strong momentum on TCV development. Initially heavily supply constrained but with 5 pipeline manufacturers, there is a need to focus on supplier base, sustainable supply, and appropriate and sustainable pricing Although treatable through antibiotics- CFR for typhoid fever in pre-antibiotic era may have been as high as 20%. Vaccines serve as a preventative measure to combat the antimicrobial resistance (AMR) threat
Portfolio balance	Cost as % of total funding	<ul style="list-style-type: none"> Gavi costs, including vaccine, VIG, and op costs by programmatic year (2019-2020) forecasted to be \$85m¹ or < 1% of total programme spend (vs v14 FF \$136m) Gavi costs, including vaccine, VIG, and op costs by programmatic year (2021-2025) forecasted to be \$865m¹ (vs v14 FF \$540m) anticipated to be < 15% of total programme spend.

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Outcome and impact	Future deaths averted per 1000 vaccinated person	<ul style="list-style-type: none"> Per IPM, approximately 0.3 future deaths averted per 1000 persons vaccinated. Within Gavi's current investments and comparable to JE. Per Yale, approximately 0.7 future deaths averted per 1000 persons vaccinated. Within Gavi's current investments and comparable to Rotavirus Yale University of Public Health model accounts for essential features of typhoid epidemiology, including waning immunity to infection and the role of chronic carriers in transmission, which is likely the driver of the difference in impact estimates.
	Impact on equity	<ul style="list-style-type: none"> Inter-country – Typhoid is largely eliminated from industrialised nations, but still affecting Gavi countries Intra-country – Vaccination will provide broad benefit to all, but it will protect those without access to safe water, improved sanitation and safe food who are at highest risk and in the most marginalised populations
Feasibility	Supplier base, product availability	<ul style="list-style-type: none"> The market is currently forecasted to be plagued by significant supply constraints until 2022, significant need to conduct market shaping activities
	Gavi market shaping potential	<ul style="list-style-type: none"> See Gavi's comparative advantage Long term commitments from the Alliance will provide additional opportunities for market shaping
	Country implementation feasibility	<ul style="list-style-type: none"> Do not anticipate extraordinary country feasibility issues New vaccine to already heavy schedule, need informed decision making to understand cost and sustainability, as well as disease burden particularly in Africa.
	Gavi implementation feasibility	<ul style="list-style-type: none"> Do not anticipate extraordinary Gavi feasibility issues Linked to above, the Alliance will work with countries to ensure appropriate prioritisation compared to Gavi's other vaccines and linkages to ongoing workstreams e.g., coverage and equity or improving quality of catch-ups

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<p>Value for Money</p>	<p>Procurement cost per death averted</p>	<ul style="list-style-type: none"> • IPM estimates \$6,580 per death averted, which is within Gavi’s current investments and comparable Rotavirus and JE • Yale estimates \$4,190 per death averted, which is within Gavi’s current investments and comparable to PCV, but estimated to be a better value for money than Rotavirus and JE. • Yale University of Public Health model accounts for essential features of typhoid epidemiology, including waning immunity to infection and the role of chronic carriers in transmission, which is likely the driver of the difference in impact estimates.
<p>Risk mitigation</p>	<p>Programmatic risk mitigation</p>	<ul style="list-style-type: none"> • Typhoid vaccination is expected to reduce the risk of multiple drug resistant (AMR) outbreaks
	<p>Market risk mitigation</p>	<ul style="list-style-type: none"> • If vaccine development timelines delayed or market shaping efforts not successful, the market will experience supply constraints, decreasing impact • Uncertain supply and demand situation could lead to strongly varying roll-out scenarios and issues with managing country demand and supply • Alliance working on roadmap with first priority to support increased supply to meet catch-up demand