Annex A: Summary of implications and risks for Gavi Alliance

Financial implications

- A Gavi Alliance programme to strengthen typhoid, cholera, meningococcus, measles, and rubella diagnostic capacity, focused on availability of improved diagnostic tools would require up to an estimated US$ 55 million during 2022- 2025. For yellow fever, US$ 5 million would be for for yellow fever diagnostic procurement and US$ 4 million for diagnostic test validation, guidance development, multi-country technical assistance, and quality assurance through the Partner Engagement Framework (PEF) Strategic Focus Area (SFA) mechanism. For cholera, meningococcus, measles, rubella, and typhoid, US$ 27 million would be for diagnostic procurement and US$ 17 million would be for PEF SFA diagnostic test validation, guidance development, multi-country technical assistance, and quality assurance. An indicative breakdown by disease is shown in table 1. In addition, US$ 2 million is needed during 2022- 2025 (i.e., US$ 500,000 per year) for Gavi secretariat coordination and monitoring of the programme, for example, programme design, application and review processes, cross-partner coordination, and programme monitoring.

Table 1: Illustrative Financial Forecast of Diagnostic Capacity Strengthening Costs by Disease for 2022-2025*

Disease	Procurement (US$ million)	PEF SFA (US$ million)
Cholera	7	6
Meningococcus	5	3
Measles	4	1
Rubella	4	1
Typhoid	7	6
Yellow Fever	5	4
Total	32	21
*Excludes any cost implications from co-financing		

- The procurement financial forecast in table 1 is based on the projected numbers of tests required to address the diagnostic gaps for the specific diseases in countries currently eligible for Gavi new vaccine support and the projected unit cost for the relevant tests. The PEF SFA financial forecast is based on the experience of the YF diagnostic tools initiative with test validation, guideline development, quality assurance, and multi-country technical assistance, adjusted for the number of potentially eligible countries and current status of laboratory networks for each disease. Typhoid, cholera, measles, and rubella diagnostic capacity strengthening will likely be relevant for a larger number of countries than for yellow fever and meningococcus, but diagnostic options for yellow fever and meningococcus will likely be more expensive. Also, the Global Measles and Rubella Laboratory Network already does a great deal of work on test validation, guidance development, technical assistance, and quality assurance which will not require Gavi funding support.

- However, savings from making Gavi targeted vaccine support programmes more efficient may help offset the costs of this programme, potentially to the extent that the savings to vaccine support programmes could be greater than the cost of the diagnostics and disease surveillance programme. The relevant Gavi targeted vaccine support programmes are forecasted to cost more than

US$ 1.6 billion during 2022-2025 (Table 2). The potential savings to Gavi vaccine support programmes may further increase in Gavi 6.0, as the relevant vaccine support programmes mature and expand and use of the expected improved diagnostic tools grows.

Table 2: Gavi Targeted Vaccine Support Programmes that Would Benefit from Availability of Improved Diagnostic Tools

Vaccine	Recommended by SAGE[1] for routine immunisation use in all areas	Recommended by SAGE[1] for routine immunisation use in only some areas	Outbreak Response Vaccination Campaigns	Preventive or Catch-up Vaccination Campaigns	Forecasted vaccine costs for 2021-2025 (US$ million)[2]	Estimated deaths averted 2021-2025[3]
Measles&Rubella[4]	Yes	No	Yes	Yes	239	~1,319k
Meningococcal	No	Yes	Yes	Yes	103[5]	~106k
Oral Cholera	No	No	Yes	Yes	199[6]	N/A
Typhoid	No	Yes	Yes	Yes	186	~316k
Yellow Fever	No	Yes	Yes	Yes	408	~606k

1. World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE)
2. Does not include forecasted vaccination campaign operational costs (US$ 362 million), Vaccine Investment Strategy vaccine operational costs (US$ 70 million), Vaccine Introduction Grants (US$ 43 million) or outbreak response vaccine costs (US$ 136 million) related to these vaccine programmes.
3. Estimates include only deaths averted through routine immunisation and preventive campaigns
4. Includes measles and measles/rubella. Rubella routine use contingent on populations being able to achieve levels of immunity sufficient to minimize risk of infection of unvaccinated females of child-bearing age. Rubella does not have an outbreak response mechanism.
5. Includes meningococcal A and Vaccine Investment Strategy multivalent meningococcal conjugate vaccine costs
6. Oral cholera vaccine includes endemic country vaccine and Vaccine Investment Strategy OCV costs

Risk implications and mitigation

- If gaps in typhoid, cholera, meningococcus, measles, and rubella diagnostic capacity are not addressed, there is an increased risk that Gavi supported vaccines will be used in areas where they are not needed and not used in areas where they are, leading to less efficient, effective, and equitable vaccination.

- The proposed Gavi effort to facilitate availability of improved diagnostic tools is purposely very focused on addressing global and regional bottlenecks in the availability of fit-for-purpose diagnostic tools and therefore needs to be complemented with other funding from domestic sources, other international sources, or Gavi Health Systems Strengthening (HSS) and Targeted Country Assistance (TCA) support. For example, such funding would be needed to address other components of disease surveillance systems such as case identification, case reporting and investigation, sample collection, data analysis, etc. Based on consultations with stakeholders, funding addressing a range of complementary needs is likely to be stable or grow across countries during this period. In addition, current and forthcoming Gavi country programme funding guidance already allows complementary HSS and TCA investments as a small portion of HSS and TCA funding plans focused on increasing vaccination of zero dose children.

- There is a risk that Gavi investments in diagnostic and disease surveillance capacity could duplicate or displace funding from other international initiatives, but extensive consultations with Gavi Alliance partners and other stakeholders during planning indicate that such Gavi investments should be complementary, and continued engagement will help to maintain this complementarity.

- There is a risk that improved diagnostic tests will prove to be technically infeasible. Consultations with researchers, manufacturers, and Gavi Alliance

stakeholders suggest that this risk is low, particularly because improved tests for cholera, typhoid, meningococcus, measles, and rubella are in relatively late stages of development and are primarily awaiting sufficient funded demand for commercial introduction as well as an effective open evaluation process for validation. Also, for several of these diseases, multiple testing technologies offer the potential for improvement over current standard tests, increasing the likelihood that at least one of them will be successful.

- Commercial failure by a manufacturer, e.g., cessation of production, is a risk. Mitigation measures to be pursued include trying to increase security of supply by having multiple suppliers for a given type of diagnostic test kit and regularly engaging with manufacturers to seek new suppliers and holding repeated open evaluations of new products.

Impact on countries

- Countries will need to fund basic diagnostic-related infrastructure, including staff, utilities, etc., to benefit from potential Gavi investments in diagnostic procurement support. Countries already provide funding for these infrastructure elements for multiple disease control programmes, so there is considerable precedent. The experience with Gavi support for yellow fever diagnostics procurement and diagnostic capacity strengthening, which does not involve cash support to countries, reinforces that many countries are already committed to provision of basic diagnostic infrastructure.

- Countries seeking to receive support through a Gavi diagnostic procurement mechanism will be required to submit applications. However, based on the experience with yellow fever diagnostic procurement support, in which 21 countries applied and were approved for such support within 9 months, the application process should be relatively short and less taxing for countries compared to applications for Gavi support for vaccine or cold chain equipment procurement, particularly given the much smaller scale of the funding provided through a diagnostic procurement mechanism.

- Countries will ultimately need to assume financial responsibility for procuring the improved diagnostic tools. All countries receiving yellow fever diagnostic procurement support committed in their initial applications to eventually assuming this responsibility. Gradually increasing co-financing can help ensure that this transition happens in an orderly manner over a reasonable amount of time.

Impact on Alliance

- As with the Gavi yellow fever diagnostics initiative authorised by the Gavi Board in 2018, an expanded effort to improve availability of fit for purpose diagnostic tools for yellow fever, typhoid, cholera, meningococcus, measles, and rubella will contribute to the Gavi Alliance's goals of providing vaccines and the means to deliver such vaccines to people in the poorest countries and helping to strengthen health care systems and civil societies supporting such purposes in the developing world. Specifically, provision of fit for purpose diagnostic tools will improve the efficiency, effectiveness, and equity of the delivery of Gavi-

supported targeted vaccines and strengthen health care systems' abilities to prevent, detect, and respond to such diseases.

- To implement an expanded diagnostics procurement support mechanism covering yellow fever, typhoid, cholera, meningococcus, measles, and rubella, the Gavi Alliance will need to expand on the existing yellow fever diagnostics collaboration. Consultations among Alliance partners indicate that such an expansion should be feasible, particularly as it will complement and draw upon existing collaborations in support of the typhoid, cholera, meningococcus, measles, and rubella Gavi vaccine support programmes.

- As with the yellow fever diagnostics initiative, implementation of an expanded diagnostics support effort will very likely require the participation of additional partners not currently involved with the Gavi Alliance. Organizations that are not involved with the yellow fever diagnostics initiative specifically and the Gavi Alliance more broadly but have a comparative advantage in key areas will be sought out and engaged. In addition, development of diagnostic target product profiles as well as guidance on how diagnostic tests can best be used to make immunisation programmes more efficient, effective, and equitable will benefit from input from and consultation with a wide range of stakeholders.

- Although partner organisations will implement most of an expanded diagnostics effort, direct Gavi secretariat involvement will be needed for multiple components:
    - Coordination of effort, including developing and overseeing requests for proposals and contracts as well as memorandums of understanding and grants to partners
    - Development of diagnostic market shaping roadmaps
    - Monitoring and evaluation of Gavi Alliance diagnostic work, including reporting back to Gavi Board on progress
    - Development and operation of Gavi processes for country applications, Independent Review Committee review, and approvals of country funding requests for diagnostic procurement funding support
    - Development and application of country diagnostic sustainability and financial transition principles