SUBJECT:	**DISEASE SURVEILLANCE AND DIAGNOSTICS TO SUPPORT TARGETED VACCINATON IN GAVI 5.0**
Agenda item:	12
Category:	For Decision

Section A : Executive Summary

In November 2018, the Gavi Board authorised creation of a Yellow Fever (YF) diagnostic tools procurement support window to operate during 2019-2021 to improve the efficiency, effectiveness, and equity of the delivery of YF vaccines and to strengthen health care systems' abilities to prevent, detect, and respond to YF. In December 2020, the Gavi Board noted that additional Gavi resources would potentially be required during 2021-2025 to similarly enhance countries' abilities to detect and diagnose other select diseases that also require rapid and targeted vaccination to prevent their spread. In light of the progress to date in improving the availability of validated commercial YF test kits, the capacity of YF public health laboratories in Africa, and the timeliness and reliability of results from those laboratories as well as the importance of those results for immunisation decision making, in June 2021 the Board authorised extension of YF diagnostic procurement support through the end of 2022 to provide time for a broader discussion of Gavi's role with diagnostic procurement and disease surveillance during Gavi 5.0. At its 20-22 October 2021and 12 November 2021 meetings, the Gavi Policy and Programme Committee (PPC) recommended an extension of the YF diagnostic tools procurement support window through the duration of Gavi 5.0 as well as its expansion to include cholera, typhoid, meningococcus, measles, and rubella.

Fit for purpose diagnostic tools are critical for countries' abilities to plan and implement targeted vaccination programmes, but there are currently market failures for such tools. This proposal addresses those market failures so that accurate, reliable diagnostic tools are available to countries and Gavi investments in these vaccine programmes, currently projected at over US$ 1.6 billion during 2021-2025, can be more efficient, effective, and equitable.

The PPC has recommended to the Board that it approve:

- Up to US$ 5 million during 2022-2025 for costs related to the procurement and distribution of **yellow fever** diagnostic test kits, reagents, supplies, and equipment and up to US$ 27 million during 2022-2025 for procurement and distribution of **cholera**, **typhoid**, **meningococcus**, **measles**, and **rubella** diagnostic test kits, reagents, supplies, and equipment, all for countries eligible for Gavi new vaccine support
- Additional funding through the Partners' Engagement Framework (PEF) Strategic Focus Area (SFA) mechanism of up to US$ 4 million during 2022- 2025 to support **yellow fever** diagnostic test validation, guidance

development, multi-country technical assistance, and quality assurance and up to US$ 17 million during 2022-2025 for **cholera**, **typhoid**, **meningococcus**, **measles**, and **rubella** diagnostic test validation, guidance development, multi-country technical assistance, and quality assurance, all through a range of global and regional partners

- Up to US$ 2 million for Gavi secretariat coordination, monitoring, and operation of Gavi's application, review, and approval processes related to diagnostic tools procurement support during 2022-2025.

Section B: Content

1. Multiple Gavi vaccine programmes involve targeting of vaccination

1.1 Of Gavi's 12 current non-COVID-19 vaccine support programmes, five involve targeted vaccines and would benefit from availability of improved diagnostic tools. Targeted vaccines are ones which are recommended for use in some areas but not others or have Gavi-funded outbreak response stockpiles or mechanisms. All of these vaccine support programmes involve preventive or catch-up campaigns targeting variable areas or age groups. Collectively, these targeted vaccine support programmes are currently forecasted to require at least US$ 1.6 billion for vaccine procurement and delivery during Gavi 5.0 (Annex 1). Three of these programmes are in their early stages, with Typhoid Conjugate Vaccine (TCV), Oral Cholera Vaccine (OCV) deployed in preventive campaigns, and Multivalent Meningococcal Conjugate Vaccine (MMCV) having been added to the Gavi portfolio during 2017-2019.[1]

2. Diagnostic gaps complicate the delivery of targeted vaccines

2.1 Vaccine preventable diseases are often clinically indistinguishable from other diseases, so timely, reliable diagnostic testing is essential for confirming whether suspected cases are in fact a specific vaccine preventable disease and thus being able to deploy the right vaccine in the right place targeted at the right people. Absence of accurate diagnostic testing can lead to unnecessary use of vaccine (i.e. wrong target population) or, alternatively, lack of use of a vaccine in an area where it would be beneficial and save lives.

2.2 In addition to the problems with availability of validated,[2] accurate diagnostic tools being addressed through the Gavi YF diagnostic tools initiative, shortcomings in the availability of appropriate diagnostic tools for

[1] The 2018 Vaccine Investment Strategy authorised Gavi support for ACW-containing multivalent meningococcal conjugate vaccines, contingent on the availability of a licensed product, outcomes of regulatory and technical review processes (including WHO prequalification and SAGE recommendation), and the meeting of specific vaccine cost targets.

[2] A validated diagnostic test is one that has been approved by a stringent regulatory body, WHO prequalified, or recommended for use on an interim basis by a WHO expert committee. Both of the latter two processes involve reviews of manufacturer's test kit performance data and manufacturing quality controls as well as an independent laboratory evaluation of a test kit's performance. Test validation helps both international and country procurement agencies identify which test kits are worth procuring and using.

cholera, typhoid, meningococcus, measles, and rubella are creating significant challenges for guiding targeting of vaccination to prevent these diseases through vaccination (Appendices 2-6).[3] Based on assessments of the diagnostic market by the Foundation for Innovative New Diagnostics (FIND) and UNICEF, validated commercial tests for cholera, typhoid, and meningococcus either are not available or are prohibitively expensive. Validated commercial measles and rubella tests are available, but they are complicated laboratory-based tests not suitable for more decentralised testing to accelerate a transition to more targeted sub-national measles preventive supplemental immuniSation activities (SIAs) in place of nationwide, non-selective campaigns.

2.3 The limitations of current diagnostic tools for cholera, typhoid, meningococcus, measles, and rubella have had important consequences for efforts to target use of vaccines against these diseases. For example, sixteen Gavi-eligible countries have not documented reliable data on diagnostic-confirmed typhoid cases since at least 1995, and many of the others only have it for a few small areas, creating major difficulties in determining which areas actually are significantly affected by typhoid and should be targeted for vaccination efforts.

3. Gavi Alliance can address global and regional diagnostic gaps

3.1 The Gavi experience with YF diagnostic tools and capacity demonstrates that the Gavi Alliance can improve the availability of validated diagnostic tools to help strengthen health care systems' capacities to prevent, detect, and respond to vaccine preventable diseases. Using its pooled procurement model led by UNICEF Supply Division (SD), evaluations of diagnostic tools organised by WHO, and technical assistance provided by a range of partners, the Gavi Alliance has facilitated the availability of a validated commercial YF test kit, with several others under evaluation, and assisted African countries at high risk for YF in strengthening their ability to confirm cases of YF in a timely manner. The rate of progress since 2018 has been particularly marked given the previous lack of validated commercial YF test kits which had persisted for years. Diagnostic test results have in turn helped make the delivery of targeted vaccines more efficient, effective, and equitable (Appendix 2).

3.2 Given the challenges that gaps in diagnostic testing create for delivery of targeted vaccines, technical working groups of staff from Alliance organisations jointly assessed which Gavi vaccine support programmes could benefit from efforts to address such gaps and how such Gavi efforts would relate to efforts to strengthen diagnostic testing capacity beyond the Alliance (Appendix 7). Based on the relevance of diagnostic tools for improving specific vaccine support programmes, the current market for relevant diagnostic tools and the potential for improvements, and added

[3] In contrast, currently available diagnostic tools for Ebola and Japanese Encephalitis seem to be largely adequate for guiding decisions on use of these vaccines in the context of Gavi vaccine support programmes (see Appendix 7).

value from Gavi efforts to improve diagnostic capacity,[4] cholera, typhoid, meningococcus, measles, and rubella were identified as diseases with gaps in the availability of diagnostic tools that warranted an Alliance effort to address those gaps.

3.3 The technical working groups identified Gavi to be uniquely positioned to address persistent gaps in diagnostic availability where these gaps are critical for delivery on Gavi vaccine programmes. Gavi can use its existing processes for engaging with countries to pool demand, to encourage countries to co-finance procurement of the relevant diagnostic tests and transition the relevant expenditures into national health budgets, and to ensure that efforts to improve availability of fit-for-purpose diagnostic tools align with the relevant Gavi vaccine support programmes and Health System Strengthening (HSS) support. WHO can assess and validate diagnostic tools, develop guidance for their use to inform vaccination strategies, and provide quality assurance and multi-country technical assistance aided by FIND, US CDC (Centers for Disease Control and Prevention), and other technical partners. UNICEF SD can apply the procurement and distribution channels used for YF diagnostic tools to other diseases.

3.4 With its pooled procurement approach that can aggregate demand over years, the Gavi Alliance can use “pull” incentives and coordinate with Alliance partners and other funders to encourage manufacturers to develop and market new products, as demonstrated by the experience with YF diagnostic tools (Appendix 2). Multiple commercial manufacturers have already indicated that a Gavi Alliance procurement initiative would be sufficient to prompt them to bring relevant tests to market for the specific diseases within scope and work to validate them despite the relatively small size of those markets (Appendices 2-6). However, bringing tests to market and the evaluations needed to validate those tests can be complicated, so substantial lead time will likely be needed between the start of the activities included in this proposal and the actual deployment of improved diagnostic tools and their impact on immunisation programmes.

3.5 The estimated costs for the extension of Gavi yellow fever diagnostics support and expansion to include typhoid, cholera, meningococcus, measles, and rubella are up to US$ 55 million during 2022-2025 (Annex A), with US$ 32 million towards diagnostic procurement based on the projected numbers of tests required to address the diagnostic gaps for the specific diseases in countries eligible for Gavi new vaccine support and the projected unit costs of the relevant tests. In addition to the diagnostic tool procurement, US$ 21 million in PEF SFA funds are requested to support identification and country use of worthwhile diagnostic tools through test validation, quality assurance, guidance development and multi-country technical assistance related to the same diseases involving a range of

[4] COVID-19 was not included in this assessment given the extraordinary nature of COVAX and the existence of the ACT-A Diagnostic tools pillar co-led by the Global Fund to Fight AIDS, Tuberculosis, and Malaria and FIND.

partner organisations during 2022-2025. Additional Gavi secretariat funding of US$ 2 million (US$ 500,000 per year) is needed for coordination and monitoring of the programme, for example, the programme design, application and review processes, cross-partner coordination, and programme monitoring.

3.6 Gavi efforts to address global and regional bottlenecks impairing the availability of fit-for-purpose diagnostic tools complement existing Gavi efforts to help strengthen health care systems' capacity through Health Systems Strengthening (HSS) and Targeted Country Assistance (TCA) funding. Gavi has long supported strengthening country disease surveillance and diagnostic capacity through these country decision making processes, with disease surveillance accounting for, on average, approximately US$ 9.3 million a year in TCA funding and US$ 5.5 million a year in HSS funding during the pre-COVID-19 pandemic years 2018-2019. Gavi country programme funding guidelines encourage Gavi support for disease surveillance activities that address specific questions to inform key immunisation programme decisions, e.g. on targeting of vaccination, and promote sustainable integration of vaccine preventable disease surveillance into broader country disease surveillance programmes as part of national immunisation plans focused on improving coverage and equity.

3.7 During the PPC's discussions of this proposal, the Norway/Finland/Netherlands/Sweden constituency representative noted that further discussion of the principles affecting Gavi Alliance's long-term involvement with diagnostic capacity strengthening as we as disease surveillance capacity strengthening would be helpful. Such a discussion can potentially be accommodated at the next Gavi Board retreat.

4. Potential impact of Gavi diagnostic tools investments

4.1 Expanding the scope of the YF diagnostic tools initiative to include other diseases would benefit multiple targeted Gavi vaccine support programmes. For example, modelling estimates suggest that accurate information on typhoid incidence to guide decision making on where and how TCV should be used would add value of US$ 95 million to US$ 193 million to the TCV vaccine support programme by better matching TCV use to areas with typhoid burden (Appendix 3).[5,6] For cholera, improved diagnostic capacity helps to better understand hotspot areas of increased risk, and this could reduce the estimated number of preventive cholera campaigns needed by half (Appendix 4).[7] Timely, reliable meningococcal diagnostic testing results would substantially improve equity of protection against meningococcal disease, particularly since the Gavi Board's 2018 VIS decision indicates that

[5] Estimate courtesy of authors of model described in: Bilcke J, Antillón M, Pieters Z, et al. Cost-effectiveness of routine and campaign use of typhoid Vi-conjugate vaccine in Gavi-eligible countries: a modelling study. Lancet Infect Dis. 2019 Jul;19(7):728-739. doi: 10.1016/S1473-3099(18)30804-1.

[6] Gavi, the Vaccine Alliance. Typhoid Conjugate Vaccine Support Window Annex B – Gavi Board Meeting 29-30 November 2017. Available at: https://www.gavi.org/sites/default/files/board/minutes/2017/08%20-%20Typhoid%20conjugate%20vaccine%20support%20window%20-%20Annex%20B.pdf.

[7] Xu H, Lee E, Azman A. The value of cholera surveillance for OCV decision making. September 2021. Unpublished.

Gavi funding for MMCV will likely be available for less than half of the individuals in the meningitis belt eligible for meningococcal A conjugate vaccine (Appendix 5). Improvements in measles and rubella diagnostic testing would allow for more timely outbreak response supplemental immunisation activities (SIAs) and accelerate the shift to targeted subnational preventive measles SIAs in place of nationwide, non-selective campaigns, potentially reducing the vaccine costs and operational costs associated with those SIAs and focusing efforts on successfully vaccinating those populations that suffer from high immunity gaps. (Appendix 6).

4.2 Improved diagnostic data, particularly for measles, will contribute to efforts to identify and sustainably reach zero dose children. As measles is highly contagious, diagnostically confirmed measles cases can more accurately highlight unimmunised and under-immunised populations. Triangulating measles cases with other data such as routine administrative and campaign coverage information can serve to both a) identify previously missed communities and gaps in population immunity and b) later confirm if efforts to reach those communities have been effective.

5. Principles for future Gavi involvement with diagnostic tools

5.1 This proposal only addresses diagnostic needs for current Gavi vaccines, excluding COVAX. Diagnostic testing may also be relevant for targeting use of future Gavi supported vaccines that will not be routinely used in all areas or will involve Gavi-funded outbreak response mechanisms. For future vaccines added to the Gavi portfolio, assessment of diagnostic capacity gaps at time of opening a vaccine support programme may be considered as part of the Board decision. The criteria used to identify cholera, typhoid, meningococcus, measles, and rubella as diseases that warranted Gavi Alliance efforts to address diagnostic capacity gaps (Appendix 7) will be relevant for such assessments. Addressing gaps in diagnostic tool availability and diagnostic capacity from the beginning of a Gavi vaccine support programme can significantly aid planning and implementation to better ensure more efficient, effective, and equitable use of the vaccines. Any Gavi efforts to address such gaps will also need to include financial sustainability and transition planning, e.g. using co-financing.

Section C: Actions requested of the Board[8]

The Gavi Alliance Programme and Policy Committee **recommends** to the Gavi Alliance Board that it:

a) **Approve** an amount of up to US$ 5 million during 2022-2025 for costs related to the procurement and distribution of diagnostic test kits, reagents, supplies, and equipment for yellow fever in countries eligible for Gavi new vaccine support through a diagnostic procurement mechanism based on Gavi's existing application, review, and approval processes;

b) **Approve** an amount of up to US$ 27 million during 2022-2025 for costs related to the procurement and distribution of diagnostic test kits, reagents, supplies, and equipment for cholera, typhoid, meningococcus, measles, and rubella in countries eligible for Gavi new vaccine support through a diagnostic procurement mechanism based on Gavi's existing application, review, and approval processes;

c) **Approve** the additional provision of up to US$ 4 million in funds through the Partners' Engagement Framework (PEF) during 2022-2025, to support global and regional efforts on yellow fever diagnostic capacity strengthening;

d) **Approve** the additional provision of up to US$ 17 million in funds through the Partners' Engagement Framework (PEF) during 2022-2025, to support diagnostic test validation, guidance development, multi-country technical assistance, and quality assurance to support effective, efficient, and equitable use of Gavi supported vaccines in countries eligible for Gavi new vaccine support as well as up to US$ 2 million for Gavi secretariat coordination, monitoring, and operation of Gavi's application, review, and approval processes related to diagnostic tools procurement support during 2022-2025;

e) **Note** the continued use of Health Systems Strengthening (HSS) and Targeted Country Assistance (TCA) funds to support surveillance and laboratory capacity in the context of national plans that focus on achieving and maintaining high immunisation coverage and address underlying equity challenges;

f) **Note** the potential inclusion of assessments of disease-specific diagnostic needs in planning of future Gavi vaccine support proposals to the Board, and potential inclusion of recommendations on addressing disease-specific diagnostic needs in these funding proposals; and

g) **Request** the Gavi Secretariat to report back to the PPC and Board on progress in 2024.

Annexes

Annex A: Summary of implications and risks for Gavi Alliance

[8] A minority position on b), d) and f) was expressed by the PPC member representing the Norway/Finland/Netherlands/Sweden constituency.

Additional information available on BoardEffect

Appendix 1: Theory of change, learning questions**,** and Monitoring and Evaluation framework

Appendix 2: YF diagnostic tools and laboratory capacity

Appendix 3: Typhoid diagnostic tools capacity

Appendix 4: Cholera diagnostic tools capacity

Appendix 5: Meningococcus diagnostic tools capacity

Appendix 6: Measles and Rubella diagnostic tools capacity

Appendix 7: Summary of assessment process of which Gavi vaccine support programmes might benefit from improved diagnostic capacity