**Supply and Procurement Roadmap**

***Yellow Fever Laboratory Diagnostic Capacity***

**The Market Shaping Goal**

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

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 **PUBLIC SUMMARY**

# Public Summary

Gavi, the Vaccine Alliance, is engaged in Yellow Fever (YF) disease surveillance, including laboratory confirmation of suspected YF cases, as a central part of its involvement in the Eliminating Yellow Fever Epidemics (EYE) Strategy. Timely, reliable identification and confirmation of YF allows more rapid containment of outbreaks and better prioritisation of preventive vaccination efforts in the face of a finite YF vaccine supply.

Major gaps in YF diagnostic laboratory capacity in countries that are at high-risk for YF currently impede the EYE implementation. Data from Gavi-funded site visits to 24 African countries considered to be at high risk for yellow fever in 2018 revealed major gaps in the capacity of the national public health YF laboratories to promptly and reliably complete confirmatory testing of samples from suspected yellow fever cases. This delays the initiation of reactive vaccination campaigns in response to YF outbreaks, which in turn allows outbreaks to cause more death, disease, and disruption than they would otherwise.

Many of the visited national laboratories reported frequent shortages or stock-outs of specific supplies, such as reagents needed to conduct initial tests for YF. In 2017, for example, 20% of samples from suspected YF cases in Africa were not tested at all due to reagent stockouts. The lack of validated commercially available YF diagnostic test kits further compounds the problem. Although commercial YF diagnostic test kits are available for YF molecular and serology testing, these currently cannot be used to confirm yellow fever cases to inform decisions about launching reactive vaccination campaigns as they lack validation of their accuracy by a reliable reviewer such as a stringent regulatory authority or the World Health Organization. This lack of validated YF test kits greatly complicates logistics for the YF national laboratories as well as efforts to ensure the quality and timeliness of testing performed at each laboratory. Without validated test kits, laboratories have to assemble all the reagents sourced separately. Invariably, stockouts of individual components may prevent testing and/or use of inappropriate reagents may render test results questionable.

In November 2018, the Gavi Board authorised allocation of funding of USD 13.5 million in support of a three-year multi-faceted programme to improve YF laboratory capacity in Africa during 2019-2021. The funding is split as follows:

1. USD 8.2 million for the set-up of a cost-effective and sustainable procurement mechanism to improve availability of reliable and quality yellow fever diagnostic tests and,
2. USD 5.2 million to provide technical assistance such as training on the use of tests, quality assurance/quality control testing to confirm the reliability of laboratories’ results, sample transportation, and laboratory network coordination in Africa.

Given Gavi’s support for the global vaccine stockpile and the costs associated with yellow fever outbreaks, the successful delivery of this programme has the potential to be cost-saving for Gavi and Alliance Partners by allowing yellow fever outbreaks to be swiftly detected and as a result contained more quickly and effectively.

**Yellow Fever Diagnostics Market Overview**

* Changes in markers of YF infection over the course of the illness require that test kits are available for both molecular testing such as PCR for testing at an early stage of infection and serology testing such as ELISA for later stage testing. Some studies suggest that the use of YF Rapid Diagnostic Tests (RDTs) is also possible and would complement a YF ELISA test in some specific situations, including during the beginning of an outbreak, in high-risk endemic regions, places difficult to reach or areas where sample transportation is weak.
* A market analysis conducted by the Foundation for Innovative and New Diagnostics (FIND) on behalf of Gavi in 2018-2019, identified a total of 37 YF test kits that are either currently available or that are in the late stages of development. The 37 test kits identified are produced by 24 different manufacturers, as follows: 15 molecular diagnostic tests (13 manufacturers), two molecular tests on integrated near patient testing (NPT) platforms (2 manufacturers), 6 ELISA kits (5 manufacturers), 5 indirect immunofluorescence assay (IFA) kits (1 manufacturer), and nine RDTs (3 manufacturers).
* In terms of regulatory status, none of the available test kits have been approved or validated by WHO or a stringent regulatory body. Most (including 6 ELISA kits), are marked as ‘Research Use Only” and few (including 5 PCR and 3 RDT kits), are self-declared CE-IVD registered (European Union Directive on In Vitro Device conformity).
* Based on the highest recorded number of YF samples sent for testing in Africa (15,000 in 2017), it is estimated that demand for YF samples testing in Africa may increase to approximately 20,000 per year within the first one to two years of an improved testing situation in the national laboratories. Considering the demand for YF testing in PAHO countries, it is projected that the global number may increase to approximately 40,000 samples per year.
* In relation to the types of tests, it is estimated that approximately 80% of samples taken in Africa would undergo PCR in addition to ELISA test (i.e. approximately 16,000/year).
* Demand for RDTs is currently unclear. Based on 2016 outbreak, RDT use is projected to likely be on approximately 10,000 samples. The closer the accuracy of the RDTs is to the accuracy of laboratory-based tests, the higher the demand for the RDTs.

Gavi’s future market shaping exit conditions: Gavi will consider its market shaping efforts on YF diagnostics successful across all relevant types of yellow fever test kits when at least one validated serology and one validated molecular YF test kit are available for procurement. This is not expected to occur before 2021, at which point Gavi will undertake an assessment to determine to what extent the problems with stockouts and delays to timely YF testing in public health national laboratories in Africa have been addressed.

**Healthy Market Framework Evaluation**

The YF diagnostic market is in a low state of health: demand is uncertain and difficult to predict given the volatility in the number of samples tested in Africa in the past 3-4 years and the market for the supply of quality-assured and reliable test kits is non-existent.

There is, however, confidence that some commercially available kits are advanced enough to pass the Alliance’s quality assurance tests and standards for procurement in the next 1-2 years.

The YF diagnostic market currently partially meets three market health attributes (highlighted in yellow - meet country preferences, long term competition and product innovation) and doesn’t meet four (highlighted in red) – buffer capacity, individual supplier risk, regulatory/quality risk and supply meets demand.

Supply meets demand: **Unmet.** There are no validated test kits available in the market; demand is uncertain, volumes may increase more than expected depending on availability of test kits & countries’ adoption.

Buffer capacity: **Unmet**: Buffer capacity will be achieved when country and global demand is better understood and reliable means to accurately project demand volumes in both routine and outbreak situations are well established.

Meet country preferences: **Partially met.** Test kits need to be compatible with laboratory platforms, our understanding is that most kits already are.

Individual supplier risks: **Unmet**. Due diligence on manufacturers’ technical production capacity and reliability is needed.

Regulatory/quality risks: **Unmet**. A quality assurance /validation process needs to be defined, test kits assessed and any quality related risks with in-field use assessed and addressed

Innovation:**Partially met**. A number of innovative approaches are currently in development; e.g. RDTs, minimizing cross-reactivity & move to panel ELISA tests, move from blood to urine samples for PCR testing

Long-term competition: **Partially met**. There are several manufacturers with available test kits with a high potential for improved competition in the future with a bigger diagnostic market including multiplex tests.

**Supply and procurement objectives**

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

* Define the quality standards for YF serology (ELISA) and molecular (PCR) tests to which the Alliance will procure from manufacturers with ‘viable’ test kits (existing and pipeline) to meet the required quality/regulatory standards
* Stimulate the supplier base to meet demand for reliable, cost-effective and quality test kits ensuring that:
	1. At least one serology (ELISA) and one molecular (PCR) test kit from at least one manufacturer of serology and one manufacturer of molecular test kits meets the Alliance’s quality standards for procurement
	2. Supply of ELISA and PCR test kits meets annual demand (covering testing of minimum 20,000 YF samples), with enough buffer capacity to absorb peaks due to outbreaks
* Improve country and global demand forecasting, facilitated by improved collection and availability of data on YF sample testing so that the proportion of samples received in national public health YF laboratories that are left untested because of supply stockouts gradually declines and eventually reaches zero
* Increase understanding of the technical breakthroughs (actual and/or projected) in potential RDT kits to replace or supplement the commercially available and validated ELISA and/or PCR test kits
* Achieve fair and sustainable prices for the test kits in line with the Alliance’s pricing targets (confidential).

**Supporting Stakeholder Action Plan**

A concerted action plan ensures the coordination between Gavi Alliance stakeholders, designed to facilitate the achievement of the above supply and procurement target outcomes. The stakeholders shall:

* Engage current manufacturers through an in-depth exploratory mission that will seek to better understand barriers to supply and to explore creatively what interventions may improve supply, develop flexibility to meet sudden increases of demand, and ensure sustainable pricing
* Define and implement test kit validation or pre-qualification criteria, standards and processes that meet the Gavi Board’s conditions for procurement
* Work with manufacturers that currently supply non-validated test kits to confirm and maintain Good Manufacturing Practices (GMP) status, validate their test kits, and potentially assure volume and reliability of supply
* Work with pipeline manufacturers to develop and validate YF test kits that are appropriate for the Gavi market
* Encourage development (actual and/pipeline) of new innovative technologies in YF sample testing and laboratory platforms
* Facilitate timely supply and delivery of validated YF test kits to national public health YF laboratories in Africa.