Gavi Strategic Goal 4

Ensure healthy markets for vaccines and related products

Supply and Procurement Roadmap Meningococcal Diagnostics Capacity

Public Summary, May 2024

Gavi
The Vaccine Alliance

Introduction

Purpose and scope

The roadmap is a foundational tool of Gavi's market shaping strategy. Its purpose is to articulate a mid- and long-term market strategy designed to align market shaping objectives and target outcomes across the Vaccine Alliance partners; define a set of interventions to reach these objectives and target outcomes; and inform procurement strategies and decisions. The objectives, target outcomes and interventions articulated in this roadmap focus on provision of meningococcal rapid diagnostic tests (RDTs) for Gavi-supported countries, while including global market considerations to highlight interdependencies and their impact on overall market health.

Current epidemiological context of meningococcal meningitis and Gavi engagement in meningococcal diagnostic tests

Meningitis is a serious infection of the meninges, the membrane surrounding the brain and spinal cord. (1,2) Meningococcal meningitis, caused by Neisseria meningitidis bacteria, is of particular concern due to its potential for large epidemics, causing severe brain damage and death in 50% of untreated cases. Meningitis causes an estimated 300,000 deaths a year globally and carries a risk of epidemics. In particular, meningitis is a major cause of death in children aged under five. The highest burden of the disease is in the 'meningitis belt' of sub-Saharan Africa, which comprises 26 countries, from Senegal in the west to Ethiopia in the east, with approximately 30,000 cases reported to the World Health Organization (WHO) each year from countries in the meningitis belt. (3)

Meningococcal serogroup A, which previously caused periodic epidemics in the meningitis belt, has been virtually eliminated from that region, with no cases reported since 2017, due to widespread use of meningococcal A conjugate vaccine. It is important to maintain high vaccine coverage to prevent a possible resurgence. Due to increases in meningitis from other meningococcal serogroups in the meningitis belt after the introduction of meningococcal A conjugate vaccine, in 2018 the Gavi Board approved the inclusion of multivalent meningococcal conjugate vaccine (MMCV) in the Gavi Vaccine Investment Strategy (VIS), with an estimated cost of US$ 895 million during 2021–2035. However, the Board required that the Gavi-supported use of MMCV be much more narrowly targeted in routine immunisation and preventive mass vaccination campaigns compared to the current use of meningococcal A conjugate vaccine.

Given the narrow scope of Gavi's planned programme expansion to include MMCV, even relatively small improvements in the effectiveness, efficiency and equity of the vaccine's use could make a substantial difference. Meningococcal diagnostic testing could be used to markedly improve efforts to reduce meningococcal morbidity and mortality through vaccination, particularly by reducing the risks of a narrow targeting approach. Gavi support for the availability and use of meningococcal diagnostic tests would address major gaps that have limited their impact on immunisation programme decision-making, such as deciding on where and when to vaccinate against meningococcal disease in a sustainable manner.

Three main types of meningococcal tests currently exist: culture, molecular and rapid diagnostic tests (RDTs), each with their own use cases and limitations. Culture testing, which is akin to a specialised craft, has uneven availability and reliability due to the time and risks involved in transporting samples of suspected meningococcal cases to laboratories and with culturing bacteria; the technical training and

skills required; the logistical challenges and costs of testing equipment and supplies; and the low sensitivity of the test, which is even lower when antibiotics are started before the sample is taken.

Meningococcal molecular tests, e.g. polymerase chain reaction (PCR) tests, have broadly similar drawbacks as culture-based tests related to sample storage, test complexity, and logistical challenges and costs, although they offer the potential for greater standardisation and scale-up among reference laboratories than culture, particularly with the expansion of PCR testing in many countries during the COVID-19 pandemic. RDTs, such as immunochromatographic lateral flow assays, could potentially be used to test closer to the patient (i.e. point of care), with a faster time to result. RDTs are simpler; require less training; and require a less complicated and expensive supply chain compared to lab-based tests.

However, no meningococcal RDTs to date have been prequalified by WHO or assessed for risk by a WHO-hosted Expert Review Panel for Diagnostics (ERPD), limiting their availability in routine testing scenarios. Illustrating the need for improved testing capacity in the meningitis belt, only 8% (6,690 out of 83,614) of meningitis cases reported to WHO from 2018 to 3 January 2021 by countries within the belt identified a causative pathogen. (4,5)

Based on WHO's estimates and expectations that annual meningococcal testing volumes will steadily increase as the availability of reliable, validated and cost-effective test kits improves, the projected addressable demand for meningococcal diagnostics (considering funding, policy and other constraints) is currently projected to be:

- up to 30,000 test kits per year from countries in the meningitis belt (all of which are also eligible for Gavi support); and
- up to 10,000 test kits per year from countries outside the meningitis belt (not eligible for Gavi funding).

Overview of meningococcal diagnostic tests market health

A 2024 review of the diagnostic market indicates that at least one meningococcal RDT is commercially available globally. (6) An expert group gathered by WHO in 2016 published a target product profile (TPP) for RDTs for the identification of multiple meningitis pathogens to be used at district-level hospitals in epidemic and endemic settings worldwide. (6) In April 2024, an updated TPP was published for a low-cost test for use in bacterial meningitis outbreak response and surveillance, reflecting expert consensus on the greatest, most urgent public health needs for diagnostic innovations to improve meningitis surveillance. (8) The TPP establishes clear requirements for manufacturers, suppliers and researchers developing new assays. Countries and procurement agencies that evaluate and select assays for use in bacterial meningitis outbreak response and surveillance may also benefit from the characteristics and associated criteria and information presented.

Although efforts by WHO and others to date provide a basis for further progress, overall the current meningococcal meningitis diagnostic market is in a low state of health. The supply of quality assured, reliable and cost-effective test kits to countries in the African meningitis belt and beyond has major limitations.

Healthy market dynamics and current challenges

The greatest challenges currently facing the meningococcal diagnostics market are:

1) ensuring supply availability from viable suppliers whose diagnostic test products meet the Alliance's standards for procurement of their products and can sufficiently meet the global demand as well as country product requirements; and
2) creating and maintaining a long-term market sufficient to sustain the interests of existing manufacturers and attract new entrants.

Although there is scope for improvement, the current meningococcal diagnostics 'market health' is categorised as unacceptable and requires further intervention, given that all high- and medium-impact 'healthy market attributes' are either unmet or only partially met.

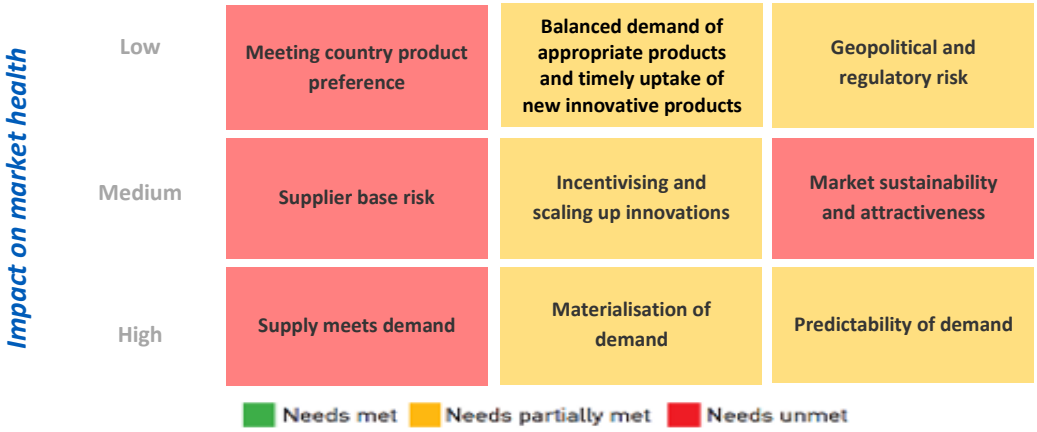
Our market health analysis indicates that five market health attributes are partially met:

1. materialisation of demand;
2. predictability of demand;
3. balanced demand of appropriate products and timely uptake of new products;
4. geopolitical and regulatory risks; and
5. product innovation.

Four attributes are unmet, highlighting concerns about availability of products that sufficiently meet global demand and varying country preferences; difficulties in adequately mitigating supplier base risk; and achieving a long-term, attractive diagnostic market.

Once a meningococcal RDT receives regulatory approval, funding is needed for the procurement and distribution of such tests. Addressing current gaps in testing is key to unlocking the potential value of high-quality meningococcal data – including diagnostic screening, confirmation and differentiation of serogroups – for targeting vaccination. Therefore, improved meningococcal diagnostics would be a valuable adjunct to Gavi's MMCV support, particularly given the current challenges of improving vaccine coverage. Gavi can fund pooled procurement to encourage diagnostic manufacturers' involvement in this market, as indicated by the experience with yellow fever diagnostics. (9-10)

Figure 1: Market health assessment 2023, based on Gavi's healthy markets framework



Materialisation of demand: **Partially met**. While demand for routine testing across meningitis-endemic countries is established, testing data reports to WHO in recent years have been relatively low compared

to reported numbers of suspected meningitis cases. For example, in 2019, 22,414 meningitis cases were reported to WHO by countries in the African meningitis belt, but only 7,980 test results were reported. Similarly,19,552 meningitis cases were reported in 2020, but only 5,173 test results were reported.

Predictability of demand: **Partially met**. Based on the current use of culture-based and PCR laboratory testing, there is evidence to suggest that demand for routine testing is established; however, volumes may increase more than expected depending on availability of more reliable, simpler-to-use, affordable test kits and adoption by countries.

Balanced demand of appropriate products and timely uptake of new, innovative products: **Partially met**. The various types of diagnostic tests (e.g. PCR, RDTs, culture) used to date for routine meningitis testing indicate a positive and widespread demand for the existing and emerging technologies to the extent that they are affordable, reliable and simpler to use. However, the current country demand assessment indicates that uptake and scale-up of new products is yet to be realised.

Supply meets demand: **Unmet**. There are no reliable and cost-effective test kits available in the market that have been prequalified by WHO or otherwise been assessed by a WHO-designated expert committee. Our market review indicates that there is one commercially available diagnostic kit approved by a stringent regulatory authority (U.S. Food and Drug Administration), but it is not sufficiently cost-effective for use on a routine basis for meningococcal surveillance, or even meningococcal surveillance quality assurance in Gavi-eligible countries.

Meeting country product preferences: **Unmet**. Test kits must be usable in settings relevant to countries – particularly rapid diagnostic tests, which can be used in low-resource, point-of-care settings without extensive consumable supplies or additional laboratory equipment. At least one commercially available RDT is currently undergoing assessment by the WHO-hosted ERPD.

Supplier base risks: **Unmet**. Due diligence on manufacturers' technical production capacity, reliability, buffer capacity, sustainability, technical risks, diversity, portfolio viability and market interest are needed.

Geopolitical and regulatory risks: **Partially met**. TPPs for low-cost tests for use in bacterial meningitis outbreak response and surveillance have been updated and published by WHO. (7) Based on these TPPs, related WHO standards for submission of dossiers from interested manufacturers for ERPD assessment have also been developed. Additionally, if other types of test kits, e.g. PCR tests, are deemed important for meningococcal vaccine support programmes, further quality assurance/validation standards may need to be defined, test kits assessed, and any quality related risks with in-field use assessed and addressed. Based on experience of test kits purchased and distributed to multiple countries to date for meningitis routine testing and outbreak responses, there is very low risk of release or export prohibitions of these and/or future test kits from the countries of production.

Market sustainability and attractiveness: **Unmet**. There are few manufacturers with commercially available test kits, indicating a high potential for increased competition and a larger meningococcal diagnostic market in the future, assuming these manufacturers' tests meet quality assurance standards. However, based on current global demand volume uncertainties, achieving a sustainable and sufficiently attractive market that offers current and prospective manufacturers the potential to realise moderate to high profit margins from fully validated (multi-serogroup) tests may be a challenge.

Incentivising and scaling up innovations: **Partially met**. A number of innovative approaches are currently available or in advanced development, e.g. single and/or multiplex PCR and RDTs used in the African meningitis belt in recent years. At least one manufacturer has been actively working to develop an RDT that can identify and distinguish meningococcal serogroups A, C, Y, W and X from cerebrospinal fluid (CSF) samples. Field tests on their product to date have shown an overall 95% sensitivity and 90% specificity, although with specificity ≥96% for some individual serogroups. A good understanding of market incentives to generate higher level of interest from other manufacturers is needed.

With Gavi interventions, the health of the meningococcal diagnostics market is expected to shift to acceptable levels in the next three to five years. This shift depends on multiple factors, including current pipeline tests successfully passing the quality assurance assessments and standards for procurement; whether those tests meet country preferences; improvements in predicting global demand for meningococcal diagnostics; sustained, long-term market attraction to existing and new players; and the impact of next-generation diagnostic test technologies on long-term competition in the global meningococcal diagnostic test market.

Strategy to sustainably improve market health

Gavi partners have defined a long-term strategy for the meningococcal RDT market to address these challenges, by reviewing different scenarios in terms of annual demand forecast for meningococcal diagnostics, available suppliers, product suitability and affordability, and long-term business sustainability. It translates into the following strategic market objectives:

Objective 1 – *Establish and maintain long-term demand for meningococcal diagnostics and generate signals of a more attractive market to suppliers with viable diagnostic products.*

Establishing and maintaining a healthy demand for meningococcal diagnostics is critical to long-term market sustainability and attractiveness to meningococcal diagnostics suppliers.

- Target outcome 1: Understanding demand for routine meningococcal diagnostic tests improves sufficiently to facilitate more steady and predictable demand by 2025.
- Target outcome 2: By 2025, meningococcal diagnostic test(s) are on the pathway to being effectively distributed to meet country demand and generate useful data to inform country immunisation programme decisions, including applications for Gavi vaccine support and requests for international outbreak response support.

Objective 2 – *Ensure supply availability and timely delivery of validated meningococcal diagnostics from viable suppliers to enable procurement and delivery to Gavi-eligible countries.*

The number of suppliers is a key driver of meningococcal diagnostics market health along the dimensions of supply availability, supply security, meeting country preferences and product adoption, regulatory and supplier risks, and long-term competition. Based on a 2022 market review, at least one RDT under development meets the minimum criteria and is currently under review by the WHO-hosted ERPD. The market review also indicates that that there are at least two manufacturers with early stage but promising innovative products, which may be available for Gavi purchase and distribution to Gavi-supported countries from 2025 onwards.

- Target outcome 3: At least one commercial test kit of a novel type, e.g. RDTs, for surveillance of meningococcus meets the TPP and WHO-hosted ERPD requirements and standards for procurement by 2025.

Objective 3 – *Scale up new and/or emerging diagnostic technologies to facilitate immunisation programme improvements, drive innovation and long-term competition, and thus stimulate competitive pricing.*

The number of new and innovative meningococcal diagnostics products is an opportunity to further shape the market and improve its health in the long term.

- Target outcome 4: By 2025, Gavi Secretariat and Alliance partners update understanding of the actual and/or projected technical breakthroughs in other meningococcal diagnostic technologies (e.g. PCR) to supplement commercially available and validated RDT test kits.

A concerted action plan ensures the coordination between Gavi and partners, and facilitates the achievement of the above strategic market objectives by:

Demand-side interventions:

- Rolling out pilot projects to better understand and define country demand for meningococcal diagnostics. Using pilot project results, work to encourage countries to better integrate testing for meningococcus into their disease surveillance systems.
- Using results from the pilot projects to encourage countries to adopt decentralised testing, including use of guidance on how best to use the RDTs to support immunisation programme decision-making.
- Leveraging the 'situation analysis' of country national plan(s) to defeat meningitis by 2030 to increase understanding of demand, deployment and use cases through mapping of meningitis diagnosis and treatment networks to at least district hospital levels within the African meningitis belt.

Supply-side interventions:

- Finalising and disseminating WHO meningococcal RDT TPPs.
- Evaluation of commercially available meningococcal RDTs by WHO prequalification team or WHO-hosted ERPD to determine if they warrant use.
- Engaging current manufacturers through an in-depth exploratory discussion to better understand barriers to supply, and to explore creatively what interventions or investments may improve supply; develop flexibility to meet sudden increases of demand; and ensure sustainable pricing.
- Accelerating work with manufacturers that currently market 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.
- Working with other pipeline manufacturers to develop and validate additional meningococcal test kits that are appropriate for the Gavi market.
- Encouraging development of new, innovative products in meningococcal sample testing and laboratory platforms.
- Facilitating timely supply and delivery of validated meningococcal test kits to target countries.

REFERENCES

1. WHO | Meningitis. WHO, 2018. http://www.who.int/emergencies/diseases/meningitis/en/ (accessed 16 January 2023).

2. WHO | Fact Sheet Meningococcal meningitis. WHO, 2018. http://www.who.int/news-room/fact-sheets/detail/meningococcal-meningitis (accessed 16 January 2023).

3. WHO Weekly epidemiological record; 3 April 2020, 95th, Nos. 14/15, 2020, 95, 133–144 http://www.who.int/wer

4. World Health Organization – Intercountry Support Team West Africa. Meningitis Weekly Bulletin Week 49–52, December 2019. Available at: https://www.menafrinet.org/sites/default/files/2020-04/Bulletin%20Meningite_S49_52_2019.pdf.

5. World Health Organization – Intercountry Support Team West Africa. Meningitis Weekly Bulletin Week 49–53, December 2020. Available at: https://www.menafrinet.org/sites/default/files/2021-01/Bulletin%20Meningite_S49_53_2020.pdf.

6. https://www.finddx.org/tools-and-resources/dxconnect/test-directories/outbreaks-test-directory/

7. World Health Organization. Specifications for a Rapid Diagnostic Test for Meningitis – African Meningitis Belt. Available at: https://cdn.who.int/media/docs/default-source/inaugural-who-partners-forum/tpp-meningitis-rdt-apr167318afd8-16ec-4048-a178-383ce3e60169.pdf?sfvrsn=a0986a29_1&download=true (accessed 30 June 2023).

8. World Health Organization (2024). Target product profile for a low-cost test for use in bacterial meningitis outbreak response and surveillance. World Health Organization. https://iris.who.int/handle/10665/376502. License: CC BY-NC-SA 3.0 IGO

9. Johnson, BW, Demanou M, Fall G, et al. Laboratory capacity assessments in 25 African countries at high risk of yellow fever, August–December 2018. Pan Afr Med J 2021; 38: 402.

10. Hampton, LM. Improving yellow fever diagnostic testing for more efficient, effective, and equitable vaccination. Sept 7, 2021. https://www.gavi.org/vaccineswork/improving-yellow-fever-diagnostic-testing-more-efficient-effective-and-equitable (accessed 6 December 2022).