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The Market Shaping Goal

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

Supply and Procurement Roadmap

Meningococcal Vaccines for Outbreak Response

Public Summary

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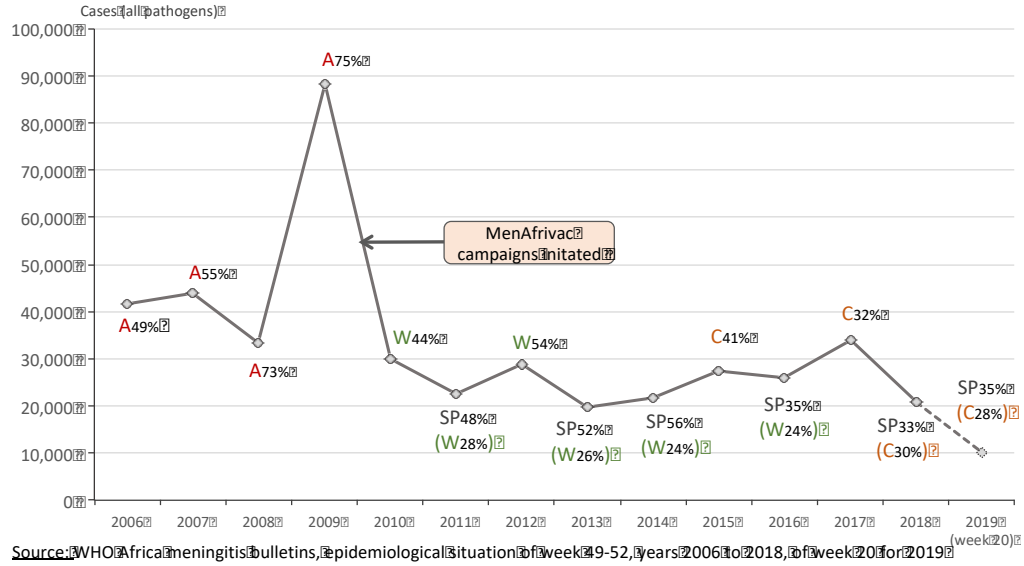
Meningococcal meningitis is associated with high fatality (up to 50% when untreated) and high frequency of severe sequelae (more than 10%) and has the potential to cause large epidemics. Meningococcal meningitis is observed worldwide but the highest burden of the disease is in the meningitis belt of sub-Saharan Africa, stretching from Senegal in the west to Ethiopia in the east.

This Roadmap focuses on outbreak response in Africa and the global meningitis stockpile managed by the International Coordination Group (ICG). The Roadmap will be expanded to include the analysis on Gavi's broader routine/campaign programme following the SAGE working group recommendations (2020).

A conjugated vaccine against *Neisseria meningitidis* serogroup A (NmA), MenAfriVac, was developed by SII with support from the Meningitis Vaccine Project (MVP) specifically to meet Gavi-supported demand to control NmA in the meningitis belt at an affordable price. Since its roll-out in 2010, epidemics due to serogroup A have almost disappeared. Following the control of NmA through vaccination, the dominant Nm serogroup shifted from NmA to NmW and NmC. Experts expect that control of NmA will be sustained until at least 2024 through continued vaccination against NmA, but they also anticipate an increased risk of meningitis epidemics in the upcoming years due to a hyper-invasive NmC serogroup in populations with low immunity.

Number of meningitis cases reported in the African Meningitis belt over 14 years 2006-2019.
The letter next to each data point indicates the dominant identified pathogen. When the dominant identified pathogen is not Nm, the dominant Nm serotype is in brackets. % refers to the % of all identified pathogens that year.



Source: WHO Africa meningitis bulletins, Epidemiological situation of week 49-52, years 2006 to 2018, of week 20 for 2019

The WHO-led "Defeating Meningitis by 2030" global strategy introduced in May 2018 at the World Health Assembly is a framework that champions meningitis control, building on the successes of regional new vaccine introductions and the elimination of NmA epidemics.

Gavi began its engagement in meningococcal vaccination in 2008 when the Gavi Board approved the strategy to eliminate serogroup A meningococcal meningitis epidemics; this was extended indefinitely in 2016. In June 2019, the Gavi Alliance Board approved in principle to expand the existing meningococcal programme to support a targeted approach that includes NmACW-containing multivalent meningococcal conjugate vaccines, subject to the availability of funding for the 2021-2025 period following Gavi's replenishment for that period, contingent on WHO SAGE recommendation and a licensed, prequalified product that meets the financial assumptions of the VIS investment case.

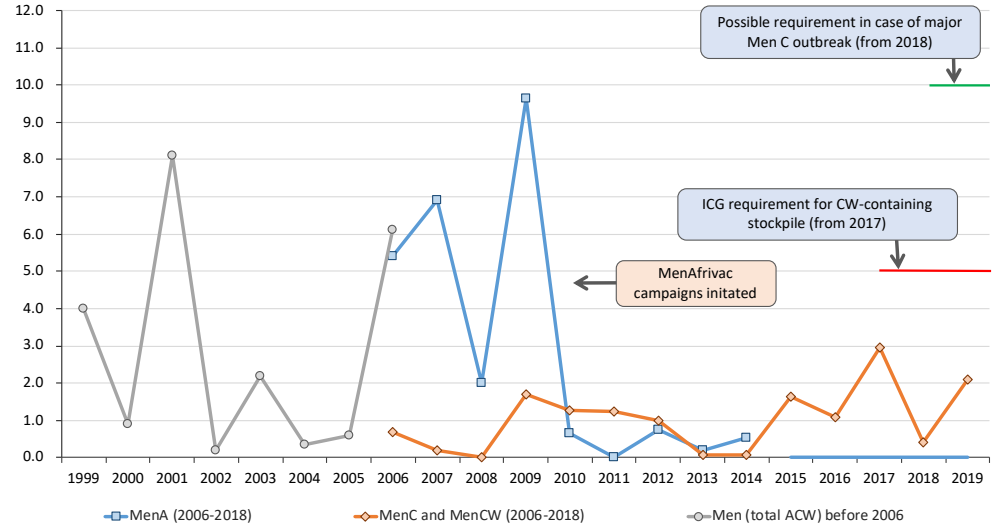
Market overview

Market volume: Over the 6-year period 2013-2018 since NmA epidemics are controlled, average annual country request was 1.8 md with a peak of 4.2 md in 2017; average annual ICG approved request was 1.2 md with a peak of 2.9 md in 2017. The International Coordinating Group (ICG) indicates the stockpile needs in volume and by type of vaccine. For the period 2019-2021, it has requested UNICEF-SD to have available a stockpile of 5md of NmC-containing vaccines at the beginning of the season, with a minimum of 3md of NmCW-containing, preferably conjugated.

Supply landscape: The current market structure is qualitatively in a position to deliver the desired types of vaccines for meningococcal outbreak response and the stockpile with three pre-qualified CW-containing conjugated vaccines, the opportunity for pre-qualification of a CW-containing polysaccharide vaccine within 3 years, and the prospect of CW-containing conjugated vaccines in development within 5 years.

However, two manufacturers interrupted the supply of 3 suitable vaccines during that last five years, offered volumes are currently insufficient to meet ICG requirements, price offers do not meet Gavi financial requirements, contracting terms required by manufacturers are difficult to accept for Gavi Partners, and most suppliers deliver less than offered or awarded.

21 years (1999-2019) supply of Meningococcal vaccines for outbreak response.



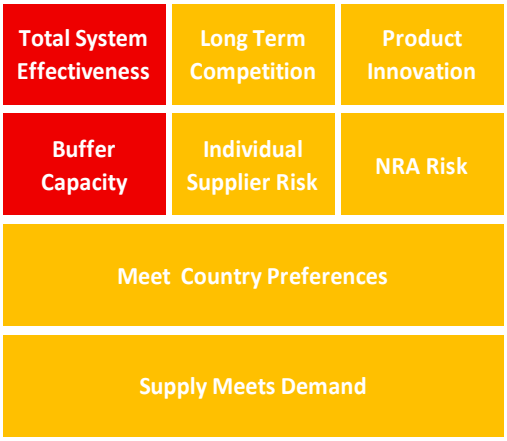
Balance of supply and demand: Worldwide, demand is higher than supply so that available supply is prioritized for HICs and is more limited where demand is uncertain and where prices are comparatively low. Manufacturers' capacity to supply volumes of vaccines appropriate for meningococcal outbreak response is likely to reach the current ICG requirement of 5md at the beginning of the season between 2021 and 2023.

Price: The UNICEF weighted average price (WAP)/dose for Nm vaccines increased from USD 0.9-2.5 between 2009 and 2014 to USD 3.9-6.1 between 2015 and 2018, and to an estimated USD 7.2 in 2019. This evolution is a function of the mix of vaccines, mainly the increasing relative proportion of multivalent conjugated vaccines following the reduced availability of multivalent polysaccharide vaccines.

Market value: The global market value (excl. China) for Nm-C-ACW-ACWY-containing meningococcal vaccines was approximately USD 1.5 billion in 2018; UNICEF accounted for less than 1% of this value market, HICs for approximately 70%, and MICs for approximately 30%. Growth 2018 over 2017 was approximately 3%.

Healthy Market Framework Evaluation

The meningococcal outbreak response market is in a low level of health in 2019 and will stay so until 2021, likely evolving towards moderate or high during the period 2022-2026, depending on key market developments. The low rating in 2019-2021 is linked to the supply not meeting the ICG requirement of 5md per year of CW-containing vaccines, and to the high prices of the available vaccines.



Currently, the meningococcal outbreak response market partly meets 6 attributes (supply meets demand, meet country preferences, individual supplier risk, product innovation, long term competition, NRA risk), and it does not meet 2 attributes (buffer capacity, total system effectiveness).

Supply meets demand: **Partially met**. Currently, supply offered to UNICEF does not meet ICG's stockpile requirement of 5md/year of CW- containing vaccines and even less the demand arising in case of a future major outbreak that may consume as much as 10md.

However, supply has met the ICG approved demand arising from outbreaks during the last 6 years. But this is to be considered in the context of ICG and country decisions integrating information on available stock, the exact impact of which is qualitatively documented. This complex and evolving situation leads to rate this market attribute as between partially met (recent country needs) and unmet (ICG demand and future outbreaks).

Country presentation preference: **Partially met.** The ideal vaccine composition, as defined currently by the ICG, is CW-containing conjugate vaccines. Currently, most available vaccines meet the CW-containing requirement but are a mix of conjugate and polysaccharide vaccines; some vaccines are C-containing only, some available presentations (pre-filled syringes) are not accepted by country/programme. The imperfect mix of available vaccines and the ICG supply-adjustments leads to rate this attribute as partially met.

Buffer capacity: **Unmet**. There is no buffer capacity compared to the ICG requirement in 2019 and none is expected to be available before 2022.

Individual supplier risk: **Partially met.** Most manufacturers have shown production and/or supply performance issues.

NRA risk: **Partially met.** NRAs related to current manufacturers are rated functional by the WHO. However, one has limited experience/track-record of release to UN organizations.

Long-term competition: **Partially met.** Short-term, about 50% of the supply is dependent on one manufacturer that has been unreliable for volume and timing over the past, and other existing manufacturers are not expected to develop a competitive market dynamic. A pipeline of 3 to 5 meningococcal vaccines may lead to new vaccines from 2022 onward.

Product innovation: **Partially met.** Most current meningococcal vaccines satisfy the ICG requirements of containing the NmCW component, and some are conjugated. However, from an epidemiological perspective an ideal vaccine should also contain the NmX serotype.

Total systems effectiveness: **Unmet.** Current conjugate meningococcal vaccines are priced unsustainably high. One conjugate vaccine is in a form of pre-filled syringe, without VVM, with high cold chain footprint (181 cm3/d). Polysaccharide vaccines offer smaller duration of protection compared to conjugates.

Supply and Procurement Objectives

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

- Supply meets the ICG defined standard stockpile needs (currently 5md/year) with NmCW-containing vaccines by 2022.
  - The highest volume manufacturer maintains GMP status and its NmACW-PS vaccine is prequalified.
  - Effective available supply increases by 30 to 50% compared to 2019 until new suppliers enter the market.
- A new Nm-ACWY(X) conjugate vaccine is WHO prequalified and available for supply to Gavi-supported countries in 2022, regardless of the magnitude of the expansion of the meningococcal programme.
- One to two other manufacturers supply a new prequalified NmCW-containing conjugated vaccine between 2022 and 2024.
- By 2022, the stockpile size reaches ICG target without exceeding Gavi's willingness-to-pay threshold based on cost/value principles (to be defined Q1 2020). In the short-term, all prices remain below the highest price currently procured.

Gavi's future market shaping exit conditions: Gavi will consider stopping its market shaping efforts on meningococcal vaccines for outbreak response when supply of NmCW-containing conjugate vaccines meets demand at sustainable prices and buffer capacity reaches 100% of the ICG requirement.

This is not expected to occur before 2023-2024.

Supporting Stakeholder Action Plan

A concerted action plan ensures the coordination between Gavi Alliance stakeholders; it is designed to facilitate the achievement of the above supply and procurement target outcomes.

- Conduct an in-depth exploratory mission that visits manufacturers to better understand barriers to supply and to explore creatively what interventions or investments may improve the supply situation and improve pricing.
- Engage the manufacturer that supplies a non-prequalified Nm vaccine to maintains GMP status, to prequalify its meningococcal vaccine, and to improve volume and reliability of supply.
- Explore whether countries that use meningococcal vaccines in their national immunization programmes could provide access to their stockpile doses under pre-arranged terms.
- Support pipeline manufacturers to develop and prequalify NmCW-containing meningococcal vaccines that are appropriate for the Gavi market to be available by 2022. Provide guidance to manufacturers as needed and appropriate to minimize time to prequalification.
- Prepare the next procurement cycle for supply 2022 and beyond.