Subject	**Gavi's role in Pandemic Prevention, Preparedness and Response: African Vaccine Manufacturing Accelerator**
Agenda item	**10b**
Category	**For Decision**

Section A: Executive Summary

Context

Following the access, equity and supply security issues experienced during COVID-19, the African Union (AU), G7 and G20 called for an international effort to improve access to medical countermeasures to better prepare for future health emergencies. This has led to support for expansion of African vaccine manufacturing. However, high startup costs mean that despite a number of headline announcements, the sustainable capacity required for supply security is unlikely to develop without complementary downstream incentives. The Secretariat has worked intensively with partners in 2023 to develop an Advance Market Commitment, now known as the African Vaccine Manufacturing Accelerator (AVMA), as part of Gavi's work to expand manufacturing capacity. AVMA has been developed via robust modelling and comprehensive stakeholder engagement, including a full range of African partners.

This paper presents a detailed proposal for AVMA. It recommends AVMA serves two core objectives: i) a sustainable African manufacturing base that contributes to healthy global vaccine markets; and ii) improved African pandemic and outbreak vaccine supply resilience. The design criteria provide time-limited incentive payments to manufacturers. It aims to leave a legacy of at least four vaccine manufacturers in Africa operating sustainably within international markets, supporting the purchase of more than 0.8 billion doses over ten years, at least three different drug substance platform technologies, and support to routine production capacity such that its repurposing could potentially yield 0.7 billion annual doses, filled and finished in an emergency. This paper highlights that AVMA is considered a 'high-risk high-reward' project and that incentivising critical actions in the broader (upstream) ecosystem under the leadership of the AU and Africa CDC will be key to success. The legal, governance, monitoring and operational arrangements for AVMA will be developed in Q1/Q2 2024.

Questions this paper addresses

- How has AVMA been developed? What is the base proposal before the Board?
- How will the governance for AVMA be developed in 2024? What are the expected impacts and risks, how are they monitored and evaluated, and risks mitigated?

Conclusions

As a critical pillar of Gavi's Regional Manufacturing Strategy and a priority for many partners including the AU, the Gavi Board is recommended to approve the

establishment of AVMA. An allocation of up to US$ 1 billion to capitalise AVMA is recommended according to the technical design and operationalisation plan.

Section B: Content

1. What is the background to AVMA?

1.1 Improving access to medical countermeasures, including vaccines, emerged as an international priority post-pandemic. Broad international support from the G7 and G20 has been reflected in new initiatives to regionalise production. Whilst the Pan American Health Organization (PAHO) is working to expand manufacturing in Latin America and the Caribbean countries, many Asian governments, including Indonesia, Vietnam, Bangladesh, Singapore and South Korea, are also investing domestically. Significant financial support is being provided by sovereign and Development Finance Institutions. Similarly, the European Union Vaccines Strategy will see additional funding earmarked for European vaccine diversification and supply security.

1.2 On the African continent, however, despite strong AU policy commitments and political support from external partners, lower volumes of financial support risk seeing the continent again impacted by supply insecurity. With Africa accounting for less than 0.1% of the world's vaccine production, yet 20% of its population, a minimum level of pandemic supply resilience is far away. Higher costs of production in the early stages of establishment will necessitate additional time-limited financial support. Any significant progress toward the achievement of the AU's target to locally manufacture 60% of the vaccine doses required on the African continent by 2040 will therefore require coordinated, rapid, substantial, and risk-tolerant investment. Many parties have a role to play. Even moderate progress towards this goal would offer a substantial dividend in pandemic resilience.

1.3 As the largest global financer of vaccines for developing countries, Gavi has committed to playing an active role aligned with its comparative advantages of market-shaping and innovative finance, across its *four-pillar regional vaccine manufacturing strategy*. This covers: a new market intelligence interface that includes clear signals on Gavi vaccine market dynamics (Pillar 1); updates to the *healthy market framework* to include regional diversification as a lever and enable new African vaccine manufacturer entrants on Gavi product menu (Pillar 2); in alignment with AU leadership, build demand solidarity from African member states (Pillar 3); and lastly, the design and operationalisation of AVMA.

2. How has the proposal for AVMA been developed?

2.1 In December 2022, the Board tasked the Secretariat to bring detailed proposals for the design and operationalisation of an Advance Market Commitment (AMC) for approval in 2023. Over the past year it has undertaken an intensive modelling and stakeholder engagement process to finalise the design of what is now known as the African Vaccine Manufacturing Accelerator (AVMA).

2.2 The Secretariat's focus has been on designing a mechanism which aligns to the AU's leadership on African Vaccine Manufacturing to support the AU's Partnership for African Vaccine Manufacturing (PAVM) Framework for Action. AVMA is designed to support a commercially sustainable industry and build pandemic supply security, whilst also safeguarding the gains of Gavi's successful 20-year model of shaping markets, improving access and lowering global vaccine prices. AVMA has been developed in close partnership with the AU and African Centres for Disease Control and Prevention (A-CDC).

2.3 Other consultations included monthly sessions with "Square Group+": Gavi Secretariat, WHO, Bill & Melinda Gates Foundation (BMGF), Clinton Health Access Initiative (CHAI), and UNICEF Supply Division; regular Civil Society consultations; and conversations with the Coalition for Epidemic Preparedness Innovations (CEPI), donors, Development Finance Institutions, and manufacturer associations. Options and funding implications have been considered by the COVAX AMC Investors Group. A Head of State-level/Africa CDC/UN General Assembly event helped raise support amongst African member states. For additional external expertise, a multidisciplinary expert reference group was convened (including industry participants, regulatory institutions, and partner organisations) to test the AVMA design. The Secretariat also hosted a two-day workshop in September 2023 with experts from the Secretariat, BMGF, UNICEF, WHO and CHAI to simulate both new and incumbent manufacturer responses and further evaluate design choices and risks.

3. What is the base proposal for AVMA?

3.1 The Programme and Policy Committee considered a set of design options for AVMA that derived from this work, based on comprehensive analysis. They recommended a base proposal for the Board to approve, with the following strategic features:

- Allowing African manufacturers **choice** to develop the routine vaccines that make sense for them and the continent by providing incentives across **all** Gavi vaccines, including COVID-19 and future Vaccine Investment Strategy (VIS) vaccines.
- **Prioritising** the development of vaccines and platforms with the greatest global benefits by offering more generous subsidies for a limited number of antigens where new entrants would be considered beneficial to global market health, and for platform technologies potentially considered of most relevance to pandemic response scenarios.
- Driving **value for money** and **sustainability** by making AVMA contingent on African manufacturers winning tenders within a standard Alliance procurement process
- Leaving a legacy of **supply security** by focussing the majority of support toward full drug substance production of vaccines, not just fill-finish.

- Stimulating **investment** and encouraging **tech transfer** from the moment of Board approval in December by announcing AVMA will be a 10-year financial instrument, capitalised with an up-front US$ 1 billion – subject to donor agreement and the availability of funding.

AVMA key terms are set out below, with further detail in Annex A. These reflect optimisations to three elements of the original base proposal, made following additional analysis and consultation, undertaken at the direction of the PPC per guidance provided at its October meeting.

Size:	Funding requirement of US$ 750-1,000 million – with the upper range set to accommodate an ambitious outcome for African products in terms of number of incentivised manufacturers and their commercial volumes
Scope:	All Gavi Alliance vaccines, Fill & Finish/Drug Product and Drug Substance (DS)
Duration:	To be launched in 2024 with a proposed 10-year duration (payments can continue for a period beyond the 10-year mark, depending on tender length)
Eligibility:	Vaccines manufactured (DS and/or Drug Product) on the African continent
Procurement pathway:	Via successful Gavi-UNICEF tenders (a potential AU pooled procurement mechanism may be accommodated in the future)
Incentive structure: *With support to Fill & Finish-only vaccines, individual manufacturers and individual single markets **capped** at 250 million of the total value of AVMA*	**Milestone payment** at WHO PQ of (i) US$ 25 million for **priority pandemic preparedness platforms (inc. potentially C19)**, (ii) US$ 20 million for **priority drug substance vaccines,** and (iii) US$ 10 million for fill & finish-only vaccines **Post-tender accelerator payment** of (i) US$ 0.50 **for priority** drug substance vaccines and pandemic preparedness platforms (inc. potentially C19), (ii) US$ 0.40/dose for non-AVMA-priority drug substance vaccines, and (iii) US$ 0.30/dose with a cap of US$1 per vial for fill & finish-only vaccines

Note: Manufacturers doing both drug substance and fill finish steps under a tender award will receive only the drug substance per dose accelerator payment for that tender.

3.2 The three amendments to the key terms included in the final proposal in front of the Board for approval are set out below, and further explained in Annex B.

- Firstly, **extending the list of 'Priority Vaccines'** where new entrants would be beneficial to global market health, (from the initial proposal of Cholera, Measles-Rubella, Malaria and Hexavalent) to include Yellow Fever and specific product profiles for three others (Ebola, Rotavirus and Pneumococcal) where such new entrants would not only be considered contributory to global market health, but, crucially, also represent a competitive asset for the manufacturer.

- Secondly, **increasing the incentive for fill-finish-only vaccines** from US$ 0.30 cents per vial to US$ 0.30 per dose, with a cap of US$ 1 vial, in recognition of the complexity of some of the steps required.

- Thirdly, at this stage, **excluding from AVMA incentives those products whose drug substance or drug product manufacturing depends on arrangements with Contract Manufacturing Organisations (CMOs).** Noting this will be subject to further analysis of these arrangements in the first half of 2024.

3.3 Gavi believes AVMA can deliver four headline impacts underneath its two foundational objectives. The first objective of helping to achieve a sustainable

African vaccine manufacturing base can be measured through: (i) at least four African manufacturers securing at least one UNICEF tender on the path to long-term sustainability; and (ii) at least 800 million vaccines manufactured on the African continent procured with support from AVMA by 2035. This means up to 20% of Gavi's African demand could be supported by AVMA – making a meaningful contribution to the AU's targets.

3.4 The second objective of improving African pandemic and outbreak supply resilience can be measured through: (i) AVMA supporting the localisation of three Drug Substance platform technologies on the continent to provide the diversity in capabilities contributory to future outbreak and pandemic response; and (ii) enabling a production capacity in Africa that could yield 700 million annual F&F doses by the end of AVMA's ten-year lifespan, when repurposed in an outbreak scenario – or enough to vaccinate 50% of the African population with a single dose.

4. Which other things need to happen in the broader vaccine ecosystem to ensure AVMA meets its objective? How will risks be tracked and monitored?

4.1 In previous PPC and Board discussions, members have been clear that Gavi's work on African regional manufacturing is a high risk, but high reward venture. The success of AVMA will rely on concerted action from wider stakeholders at local, regional, and global levels, to create the necessary regulatory, policy environment, investment, technology transfers, and demand required to build a sustainable vaccine industry. No single organisation can deliver across the full ecosystem. Important responsibility will lie with Africa CDC and African institutions to help coordinate support and monitor progress – as well as ensuring African Member States remain supportive, and make commitments to select and purchase vaccines made in Africa supported by the mechanism.

4.2 The Secretariat has spent significant time identifying risks to the success of AVMA. A proactive risk management and monitoring strategy will form part of AVMA's governance (as described in section 5). The Secretariat's strong view is that the existence of AVMA will help shine additional light on otherwise overlooked bottlenecks. The goal will be to engage new and influential stakeholders and help channel accelerated support to these key parts of the enabling ecosystem, where necessary, including across the following 5 categories of risk:

4.3 Firstly, the enabling regulatory environment has been highlighted by many stakeholders as a priority bottleneck to address: the establishment of the African Medicines Agency; continued progress of more African National Regulatory Authorities (NRAs) towards the WHO Maturity Levels necessary for oversight of manufacture of Prequalified vaccine; and ensuring that WHO's Prequalification (PQ) processes are equipped to process an influx of applications from the continent. The Alliance has a key role.

4.4 Secondly, adequate country demand is another critical enabler. For AVMA to be successful, African countries will need to buy the vaccines once they appear on the Gavi menu. The Secretariat is committed to ongoing work with the AU and Member States on demand solidarity under Pillar 3 of Gavi's Manufacturing Strategy.

4.5 Thirdly, minimising unintended impacts on vaccine markets and prices. The base proposal for AVMA has been designed to lower risks by clearly signalling which antigen markets benefit from additional entrants. In addition, incentives have been designed to ensure manufacturers bid at competitive prices, offsetting additional costs they face compared to incumbents. Sensitivity analysis on Gavi's core budget range from AVMA having a net favourable (negative) impact of -US$ 50 million over 10 years to an unfavourable impact of around +US$ 250 million on overall procurement (during AVMA's lifetime).

4.6 Fourthly, manufacturer risk. Vaccine manufacturing is complex, and the AU's targets are ambitious. Manufacturers facing catastrophic cashflow crises before winning tenders may never benefit from the AVMA per dose incentive. This would result in the underutilisation of AVMA, and unrealised continental aspirations. This risk is partially mitigated by the inclusion of AVMA milestone payments on the achievement of WHO PQ. This rewards intermediate progress with a view to bolstering both medium and longer-term sustainability.

4.7 Fifthly, incorrect design of AVMA and its incentives. Incentives could be insufficient to bridge funding gaps faced by African manufacturers. Conversely, if incentives are too generous, or they do not drive the localisation of technology in Africa, AVMA will carry significant reputational risk. The Secretariat has attempted to mitigate this risk through substantial modelling and analysis, comprehensive consultation and the proposed governance arrangements.

5. How will the Secretariat finalise AVMA's governance and monitoring arrangements in 2024?

5.1 Should the Board agree to approve the establishment of AMVA, the Secretariat recognises there is much work to do in 2024 to finalise appropriate governance, legal and operational details for AVMA prior to launch. Discussions at the PPC focussed heavily on this point, and members requested further information to be provided to the Board in the first half of next year.

5.2 The Secretariat is proposing to follow best practice for Board-approved financial instruments and will draw on lessons from instruments such as the PCV AMC by taking a principles-based approach to developing the arrangements for AVMA in 2024. This will require an inclusive steering committee, designed to allow donors, technical experts and key partners such as the Africa CDC to play an appropriate role. AVMA will also need to dock in closely to the broader African manufacturing ecosystem as highlighted in the previous section. A high-level mapping of key dependencies related to regional demand, regulatory strengthening and pre-qualification functions at WHO will help ensure that AVMA is linked into broader AU and Africa CDC networks, such as future

"manufacturers' marketplace" meetings, as well as relevant international initiatives, such as the EU's "Initiative on manufacturing and access to vaccines, medicines and health technologies in Africa" (MAV+).

5.3 AVMA is proposed as a 10-year mechanism, and whilst the draft Monitoring, Evaluation and Learning framework and theory of change set out key objectives, impacts and outcomes – there will be a clear need for interim milestones to be established alongside a regular reporting process prior to launch. In addition, the Secretariat intends to set out a carefully structured process for reviewing key terms of the mechanism to enable a mid-course correction and the ability to respond to external factors and changes in a fast-moving external environment. This process will be designed by the Secretariat with cross-functional input to ensure that the scope and frequency of potential changes are clear in advance, so as not to undermine the incentive effect of the mechanism for manufacturers and investors. For the Treasury function, there are two options under consideration – either managing AVMA funds internally via Gavi Treasury or collaborating with an external bank to manage the funds – a role that was played by the World Bank for the PCV AMC.

5.4 The Secretariat will finalise the governance details in the same spirit of open stakeholder consultation used to define the key design criteria for AVMA to date. This finalisation process will include further analysis of legal and regulatory risks as well as the development of the necessary documentation between Gavi, external partners and manufacturers as required to operationalise AVMA.

6. Conclusion

6.1 Following the adoption of the first three pillars of Gavi's Regional Manufacturing Strategy by the Board in December 2022, stakeholders across the African Vaccine Manufacturing ecosystem have been eagerly awaiting the development of Gavi's AMC – in recognition of both the financial significance of Gavi on the African continent and of the signalling power of the Alliance. Board approval of the key design criteria for AVMA as recommended by the PPC and set out in detail in Annex A would send an immediate investment signal of Gavi's long-term commitment to manufacturers and investors, such as the Development Finance Institutions and other potential providers of capital.

Section C: Actions requested of the Board

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

a) **Approve** the establishment of the African Vaccine Manufacturing Accelerator (AVMA) as an instrument to provide time-limited financial support to accelerate the expansion of commercially viable vaccine manufacturing in Africa, in accordance with the key terms in the base proposal set out in Annex A to Doc 10b, as amended in follow up to discussions at the PPC;

b) **Note** that this approval is contingent on available funding from the COVAX Advance Market Commitment (AMC) Pandemic Vaccine Pool (PVP) as confirmed by the Gavi Audit and Finance Committee. Under the base proposal, a capitalisation of up to US$ 1 billion is required;

c) **Note** that the investment proposals were developed with full consideration of enhanced collaboration with other pandemic recovery and PPPR initiatives and considered by the COVAX AMC Investors Group, as requested by the Board in June 2023, and were supported as options for the use of COVAX AMC PVP funds; and

d) **Request** that the Secretariat brings back to the Board the following in the first half of 2024: further analysis of legal and regulatory risks relating to the provision of Gavi's support; the articulation of intermediate milestones and review points; the establishment of a Treasury function; proposed governance arrangements with related legal terms and conditions established; and a high-level mapping of key dependencies related to regional demand, regulatory strengthening and prequalification functions at WHO.

Annexes

Annex A: AVMA Base Proposal – key terms

Annex B: Details of key terms amended in follow up to PPC discussions