

## Annex B: Design considerations for an Advance Market Commitment to support sustainable vaccine manufacturing capacity

The Secretariat is currently exploring different options for the following AMC design considerations:

1. AMC objectives
2. Value chain focus
3. Incentive structure
4. Antigen specificity
5. Procurement pathway and manufacturer eligibility
6. Financing, governance and operationalisation

Given the number of interested stakeholders and range of model options, the Secretariat is facilitating a transparent and evidence-based treatment of these design options to facilitate constructive open debate. These analyses reflect substantial learning from the PCV AMC and explore the implications of multiple design choices on operationalisation and impact. Further analysis and expert validation are being conducted over Q3/4 2023 before any recommendations are made.

### 1. AMC objectives

To strengthen regional manufacturing of vaccines the Gavi Board approved three underpinning objectives in December 2022. The AMC mechanism is expected to adhere to these as “boundary conditions”:

Gavi board-approved objectives	Description
<b>Support healthy global markets</b>	Minimize market distortions and help to sustain low global prices and resilient supply for priority vaccines
<b>Drive efficient market outcomes</b>	Provide a signal to guide and align new manufacturers and investors behind resilient, sustainable business propositions
<b>Reduce barriers to investment</b>	Carefully structuring the level of incentive to help offset initial costs of market entry whilst aligning support with other providers of capital for greater overall impact

These have been translated into two clear overarching AMC objectives, that both meet Gavi’s objectives and match the requirements of external stakeholders voiced during the Secretariat’s consultations (in order of priority below). Drafting theories of change for these AMC objectives has already begun. These will form the foundation of a holistic monitoring, evaluation and learning strategy to accompany the AMC as well as the broader four-pillar regional manufacturing strategy. Gavi is also embracing learnings generated from other AMCs as part of this design process.

Proposed design objectives	Rationale for proposal	Potential implications for the AMC design
<b>A) Regionally diversified vaccine supplier base:</b> Contribute to a substantial, sustainable manufacturing base in Africa	<ul style="list-style-type: none"> <li>• Reduces barriers to investment and enables the development of local vaccine manufacturing industry. This subsequently builds local biomedical capabilities (including for R+D), drives local sector development (including to address other NTDs), and</li> <li>• Incentivises global healthy market dynamics, i.e. sustain low global prices and resilient supply for priority vaccines</li> <li>• Drives efficient market outcomes by focusing vaccine manufacturers toward sustainable business models, to ensure long-term impact beyond duration of the AMC mechanism</li> <li>• Incentivises the work towards building the regional and national regulatory quality, plus the human capital development and the supplier base necessary for the industry.</li> </ul>	<ul style="list-style-type: none"> <li>• Set the right incentive level and structure to positively tip the risk-balance for investors and manufacturers, while also ensuring sustainable exit for the mechanism</li> <li>• Set guardrails to ensure geographic distribution, broad antigen coverage, and variety of manufacturers (e.g. by setting specific caps)</li> <li>• Focus on localising both DS as well as F&amp;F (likely stronger short-term focus on F&amp;F to build an initial local base)</li> </ul>
<b>B) Improved pandemic preparedness, and response:</b> Contribute to a diversified manufacturing capacity to improve supply	<ul style="list-style-type: none"> <li>• Aligns with ongoing momentum and political support following COVID-19 pandemic, where Africa did not enjoy early equitable access to COVID-19 vaccines from global manufacturers.</li> </ul>	<ul style="list-style-type: none"> <li>• Prioritize localising both DS as well as F&amp;F (likely stronger focus on DS for PPR purposes)</li> <li>• Diversify across several platform technologies to ensure a diversified</li> </ul>

capacity and resilience; improving access and lowering prices in future pandemics	<ul style="list-style-type: none"> <li>• Supports healthy global markets to ensure supply resilience against vaccine nationalism, whilst increasing supply capacity to help sustain lower prices during 'surge' pandemic demand.</li> <li>• Contributes to improved health security and health security sovereignty</li> <li>• Aligned with Gavi 5.1 which includes broader role for Gavi in pandemic preparedness, and response</li> </ul>	<p>portfolio of production capacity and capabilities</p> <ul style="list-style-type: none"> <li>• Incentivise platform technologies with flexibility, scale-up potential, and rapid development timelines to enable a response to threat X</li> </ul>
---	---	---

## 2. Value chain focus

To reach the two proposed design objectives, the AMC is expected to support end-to-end production of vaccines on the African continent, i.e. substantial Drug Substance (DS) production. However, Fill and Finish (F&F) could offer value to reach the AMC objectives. The transition to DS production will likely take time, and there is expected significant value in incumbent (non-Africa-based) manufacturers providing licencing and tech transfer arrangements which may enable rapid local F&F capacity in an interim period, transitioning to full DS over time.

Different incentive structures (e.g. higher per dose incentive level for DS) as well as potential caps (e.g. limiting the AMC to a certain volume for F&F to ensure sufficient incentive for DS) are being explored.

A non-exhaustive outline of possible options for the value chain focus are summarised in the table below:

Options	Considerations
<p><b>End-to-end localisation</b></p> <p>The AMC supports vaccines produced end-to-end, including DS and F&amp;F (e.g. with different incentives)</p>	<ul style="list-style-type: none"> <li>• DS localisation will likely require more time, given the dependency on external factors, but may be bridged in the interim with F&amp;F support</li> <li>• More likely to meet the expectations of African stakeholders</li> <li>• Enables superior pandemic preparedness and health security due to real self-sufficiency</li> <li>• Would need to address significantly higher, and more variable DS production cost structure</li> </ul>

<p><b>DS-focused AMC</b></p> <p>The AMC provides incentives for manufacturers producing drug substance in Africa</p>	<ul style="list-style-type: none"> <li>• DS localisation will likely require more time, given the dependency on external factors.</li> <li>• Would need to address significantly higher, and more variable DS production cost structure.</li> <li>• For real self-sufficiency and improved pandemic preparedness localised F&amp;F is required as well</li> </ul>
<p><b>F&amp;F-focused AMC</b></p> <p>The AMC provides incentives for manufacturers in Africa that import drug substance from international manufacturers and do F&amp;F</p>	<ul style="list-style-type: none"> <li>• F&amp;F focus may allow to disburse incentive earlier and therefore may have a faster timeline for impact</li> <li>• F&amp;F potentially simpler to design as similar COGS structure assumed across antigens and platform technologies</li> <li>• Potentially less likely to promote the development of DS manufacturing capacity and novel products for unaddressed diseases</li> <li>• Less impact on health security</li> </ul>
<p><b>Discussion:</b> The AMC is expected to support end-to-end production of vaccines on the African continent, i.e., including Drug Substance (DS) production, to improve real self-sufficiency and reach the two proposed objectives. Other individual value chain steps are being explored further.</p>	

### 3. Incentive structure

The Secretariat is currently exploring several design considerations for the incentive structure of the AMC.

The AMC is expected to pay a top-up incentive per dose. The incentive level could be designed as an absolute number per dose (e.g. x Cent per dose), a payment proportional to the price (e.g. x% of the price), or a hybrid model. Potential unintended consequences might arise through the design of any incentive structure that allows the disproportionate or inequitable allocation of funds. Therefore, the Secretariat is currently exploring potential caps by country, product and/or manufacturer. Further modelling of the implications as well as stakeholder alignment will be conducted to determine the best structure to mitigate these consequences.

A non-exhaustive outline of possible options for the incentive structure are summarised in the table below:

Options	Considerations
<b>Incentive as % of price</b> The incentive is calculated as a percentage of the Gavi Weighted Average Price (WAP)	<ul style="list-style-type: none"> <li>• % of price may better capture the dynamic development of markets over time</li> <li>• % of price may incentivise manufacturers to raise prices; could potentially be mitigated by need to win competitive tender and basing incentive on WAP instead of manufacturer price</li> </ul>
<b>Incentive as absolute incentive</b> The incentive is capped as an absolute incentive to be added to the price, independent of the price level	<ul style="list-style-type: none"> <li>• An absolute incentive may give manufacturers more clarity with regard to the value of the incentive to be expected</li> <li>• An absolute incentive could preclude certain antigens with low margins and high COGS, such as e.g. HPV and PCV</li> </ul>
<b>Hybrid model</b> Different incentive structures are leveraged for different purposes (e.g. absolute incentive for F&F and proportionate for DS)	<ul style="list-style-type: none"> <li>• A combination of both, a proportionate and absolute incentive, might allow a higher level of flexibility to set the right incentive level across value chain steps and/or product groups</li> </ul>
<b>Discussion:</b> Current modeling indicates that a hybrid model might reflect best the reality of differentiated cost structures and business cases (e.g. an absolute incentive might be more applicable for F&F and a % of the WAP for DS, considering the limited COGS difference for F&F compared to DS manufacturing). Nevertheless, careful considerations and further validation is necessary to mitigate any unintended consequences through the incentive design.	

#### 4. Antigen specificity

The AMC may be open to all antigens that bid successfully in any tenders for a WHO pre-qualified Gavi vaccine manufactured by an African-based manufacturer (see country and manufacturer eligibility below) or only support a selected group of antigens. Differentiated incentive payments for selected antigen categories could be considered during the AMC design, with a specific focus on improving overall global vaccine market health, supporting sustainable business models, and supporting a diversity of technology platforms that may be scaled for pandemic response.

A non-exhaustive outline of possible options for the antigen specificity are summarised in the table below:

Options	Considerations
<b>Open AMC</b> All antigens can be supported by the incentive	<ul style="list-style-type: none"> <li>• Simpler design that may enable manufacturers and investors to account for the incentive with higher certainty in their business cases</li> <li>• May reduce perception of winner-picking</li> <li>• More complex to define appropriate incentive value across wide range of antigens</li> <li>• AMC structuring takes place without full view of complex commercial considerations facing investors / manufacturers, could hinder development of nascent industry.</li> </ul>
<b>Targeted AMC</b> Only certain antigens can be supported by the incentive	<ul style="list-style-type: none"> <li>• May allow for active market shaping and more supporting for antigens considered to have a market health need or relevant for PPR</li> <li>• Could incentivise new industry developments (e.g. new vaccine for unaddressed disease)</li> </ul>
<b>Discussion:</b> Both options could likely be deployed to achieve the proposed objectives of the AMC. Further work will examine whether aspects of a targeted approach could be implemented without raising too much complexity or investment uncertainty. In either scenario, Pillar 1 is expected to help mitigate against the development of unbalanced regional portfolios.	

## 5. Procurement pathway and Manufacturer Eligibility

AMC eligibility considerations include (a) which procurement pathways, and (b) which manufacturers are eligible to benefit from the AMC.

### a) Procurement pathway eligibility

The AMC may provide an incentive per dose to African Vaccine Manufacturers that successfully win volume through Gavi Alliance tenders. This would ensure that the instrument incentivises investors to bid (and win) competitive tenders—through established and transparent processes. A transparently published incentive payment would potentially enable new manufacturers to factor this offset into their bids and assist their cost structure.

In addition to the Gavi Alliance tenders, the mechanism could be structured so as to be inclusive of any future AU procurement mechanism, and potential bilateral volumes, if technically and legally feasible (understanding that some volume may not be logistically possible to include e.g. volumes from countries that do not procure through Gavi Alliance tender process, such as never-Gavi countries/HICs). Further assessment of practical and legal implications of country procurement outside of Gavi Alliance tender is required to determine how expansive the AMC can be in terms of whose demand is covered.



A non-exhaustive outline of possible options for the procurement pathway eligibility are summarised in the table below:

Options	Considerations
<b>Gavi Alliance / UNICEF volumes</b> Vaccine products procured through Gavi Alliance / UNICEF tenders are eligible	<ul style="list-style-type: none"> <li>• Most administratively and legally feasible option</li> <li>• Least or no financial/reputational risks</li> <li>• Likely limiting demand generation</li> <li>• Demand may further reduce over time as transitioned countries may no longer procure via UNICEF (potentially due to handling fee)</li> </ul>
<b>Future AU procurement mechanism</b> Gavi supported vaccines procured through a future AU procurement mechanism are eligible	<ul style="list-style-type: none"> <li>• Demonstrating Gavi's support for AU initiative</li> <li>• Technical and legal feasibility to be explored</li> <li>• Still potentially losing demand from transitioned countries</li> <li>• AVAT / AU Pooled Pilot at exploratory stage of development for non-COVID-19 vaccines</li> </ul>
<b>Bilateral volumes (from products that were successful in UNICEF tenders)</b> All vaccine volumes from a manufacturer for products that were successful in a Gavi UNICEF tender are eligible (incl. bilaterals outside the UNICEF tender)	<ul style="list-style-type: none"> <li>• Gavi WAP can be reference price for bilateral volumes</li> <li>• Enables broadening country scope to incl. Gavi transitioned and Never-Gavi countries purchasing Gavi-approved products bilaterally</li> <li>• Challenge of accountability for manufacturer's reported volumes</li> <li>• Technical and legal feasibility to be explored</li> </ul>
<b>Including all bilateral volumes</b> All vaccine products winning tenders are eligible	<ul style="list-style-type: none"> <li>• Likely maximises demand volumes applicable for the AMC</li> <li>• Most risky option as Gavi does not have leverage over transactions happening outside of Gavi Alliance tender scope</li> <li>• Technical and legal feasibility unclear</li> <li>• Lack of transparency over prices for products that did not win Gavi Alliance tenders (resulting in potential lack of competitiveness)</li> </ul>
<b>Discussion:</b> The current hypothesis is that most or all volumes from Gavi Alliance / UNICEF tenders may be eligible for the AMC. In addition, volumes from a future AU procurement mechanism, as well as bilateral volumes of Gavi eligible vaccines (from manufacturers that were successful in Gavi Alliance / UNICEF tenders) will be further explored for technical and legal feasibility.	

## b) Manufacturer eligibility

To contribute to a substantial and sustainable manufacturing base in Africa, it is important to consider which vaccine manufacturers would be eligible for the AMC incentive.

A non-exhaustive outline of possible options for manufacturer eligibility are summarised in the table below:

Options	Considerations
<b>Full local player</b> Africa-based manufacturer with DS/F&F production locally on the continent	<ul style="list-style-type: none"> <li>• May contribute most to AMC objectives</li> <li>• Potentially long lead times to establish DS (likely dependent on a bulk provider for an interim period)</li> </ul>
<b>International manufacturer localising F&amp;F/DS capacity</b> International PharmaCo localising F&F/DS capacity on the African continent	<ul style="list-style-type: none"> <li>• May be most efficient way to localize manufacturing capacity given existing expertise and capabilities</li> </ul>
<b>Company employing African CMO</b> CMO in Africa conducting F&F and/or DS, product sold under name of contracting manufacturer which receives incentive	<ul style="list-style-type: none"> <li>• Existing manufacturers could leverages CMOs to conduct a value chain steps in Africa to receive the incentive</li> <li>• May indirectly create more business opportunities for African CMOs</li> <li>• Products are labelled and sold by the contracting manufacturers, potentially minimizing local capabilities</li> <li>• Might be challenging to track which volume was produced with which CMO</li> </ul>
<b>Secondary packaging</b> Manufacturer only conducts secondary packaging in Africa	<ul style="list-style-type: none"> <li>• Secondary packaging is likely a too little value-adding step to aid Gavi's objective of localising vaccine manufacturing and aiding pandemic preparedness</li> </ul>
<b>Discussion:</b> There is clear stakeholder support for the AMC to be current as inclusive as possible for vaccine manufacturing activity on African soil (except secondary packaging, because it is likely not contributing sufficiently to the AMC objectives). Nevertheless, the Secretariat will further assess different business models and align potential eligibility criteria with co-creation partners, including the AU, Gavi governance, potential donors and implementors.	



## 6. Financing, governance, and operationalisation

The Secretariat is working on a proposed governance structure as well as a view on the instrument timeline. Financing for the AMC would be discrete from Gavi core funds. A mixture of upfront and flexible funding is foreseen. The AMC will likely need to have access to funds upfront, but due to regulatory and demand uncertainties, final disbursement timing may be hard to predict. Therefore, there is a clear need for a treasury function to manage multi-year commitments from donors.

### Enablers required to ensure AMC success

The AMC is just one part of the broader ecosystem to enable African vaccine manufacturing. The Secretariat has worked to align to regional frameworks and focus on Gavi's specific role, mandate and added value. In terms of the broader ecosystem, the Partnership for African Vaccine Manufacturing (PAVM) has identified eight priority areas: (1) Market design & demand intelligence, (2) Access to finance, (3) Regulatory strengthening, (4) Technology transfer and IP, (5) Research & Development, (6) Talent development, (7) Infrastructure development, and (8) Agenda-setting and coordination.

The AMC is expected to contribute substantially to priorities 1 & 2 of the above. However, concerted action by partners will be critical if the AU's ambitions are to be realised. Most critical of these will be, firstly, support to the regulatory landscape across the continent to facilitate the inclusion and procurement of new vaccines. Secondly, the development of a regional demand pact, to further reduce the risks facing investors, and send clear signals around market opportunities for priority antigens. The Secretariat is in dialogue with Africa CDC, Alliance and other partners to as far as possible, maximise joined up support across this agenda.

### Next Steps

Detailed modelling work together with extensive internal and external expert consultations, including with Africa CDC and technical experts (e.g. on vaccine manufacturing, vaccine economics, among others), will inform and validate the AMC design further. Following a further consultation process (and critically interest from donors), details of a prospective proposal will be shared with the Gavi PPC and Board for further refinement and any decisions on programmatic issues in late 2023.