White Paper

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A New Era of Vaccine Manufacturing in Africa

Contents

Executive summary

One of the prominent issues exposed by the COVID-19 pandemic is the urgent need to further diversify global vaccine manufacturing, particularly with regards to Africa. With the political realities of nationalism, trade barriers, and the absence of regional manufacturing capability and capacity, rapid and equitable global access to life-saving vaccines can be compromised, leading to delays that put lives at risk. We cannot rely on market forces to provide secure supply during a pandemic. As seen with COVID-19, this has particularly been the case in Africa. According to the World Health Organization (WHO), Africa has fewer than ten vaccine manufacturing facilities, of which only one produces a vaccine prequalified by WHO, a requirement for vaccine-procuring United Nations (UN) agencies and global health organisations, including Gavi, the Vaccine Alliance. This leaves African nations inherently reliant upon imports of vaccines from other regions, for COVID-19 vaccines, future pandemic vaccines and also for almost all the routine vaccines used to prevent infectious diseases that are prevalent in the region.

This scenario can be changed, and with more than 20 new initiatives aimed at expanding vaccine manufacturing within Africa, that is already happening. These developments are an extremely timely opportunity to improve health security for people across the continent, and a chance to further improve the health of global vaccine markets with additional suppliers for a wide range of vaccines. Success, however, cannot be taken for granted. This expansion needs to be built around a shared vision and work-plan focused on achieving long-term success and sustainability. As the world's largest purchaser of vaccines, the largest purchaser on behalf of lower-income countries and the engine at the core of COVAX, Gavi, the Vaccine Alliance, has a critical and active role to play in working with African countries, the African Union (AU) and continental structures to realise that vision.

Understandably, much of the current attention – political and financial – is on the production of COVID-19 vaccines. However, ultimately, the biggest health and economic gains will in fact come from the production of other life-saving vaccines for which there will be more certainty of long-term demand. This broader focus is also important for achieving sustainability. COVID-19 is currently a crowded market and a view on long-term demand has yet to be established. Therefore, the future of supply resilience is likely to rest with non-COVID vaccines of regional importance. Creating facilities capable of producing vaccines against infectious diseases like measles, rubella, cholera and malaria, as well as other diseases for which no vaccines currently exist, has huge potential to increase the global supply of such vaccines, and therefore protect more people from deadly and debilitating diseases in Africa and beyond. In doing so, it will also serve to establish a sustainable vaccine manufacturing industry in Africa that could stand ready to be redeployed in times of crisis to produce pandemic vaccines, if or when the need arises.

Building a vibrant African vaccine manufacturing industry requires capital investment, (public and private), technology and know-how transfer, and business strategies that align production capacities with the expected vaccine demand. In parallel, quality assurance, stringent and independent regulatory review, resilient supply chains, and other supportive industries and systems will need to be in place. These priorities are at the centre of the goal and strategy of the AU and the Partnership for African Vaccine Manufacturing (PAVM), to achieve a target for Africa to manufacture at least 60% of its routine immunisation needs within the continent by 2040. Equally important will be the need for rigorous analysis of which antigen markets should be targeted (beyond COVID-19), with a focus on complementing global market health needs, on vaccines of regional importance and on novel vaccines and unaddressed diseases wherever possible. All this will be important for the long-term success of Africa's vaccine manufacturing industry.

As an important vaccine funder, and with the experience of designing long-term innovative financing mechanisms to promote sustainable diversification, Gavi is well placed to support the broader effort to achieve supply resilience and establish African manufacturers as substantial and sustainable suppliers of vaccines to all Gavi-supported countries, both in Africa and beyond. This report explores both the potential gains and the challenges at play, and how Gavi is now working proactively with partners, including the AU and PAVM, on how it can support and work towards a shared vision for sustainable regional manufacturing.

1 The need for health security in Africa

In the 18 months since COVID-19 vaccines were first licensed, nearly 12 billion doses have been administered to people around the world, enough to protect everyone on the planet. During this time COVAX, the partnership aimed at making access to these vaccines equitable, delivered more than 1.5 billion doses to 146 economies, with more than 90% of these going to people in lower-income countries. Yet while COVAX was able make COVID-19 vaccines available to lower-income countries within just 39 days after people in high-income countries first received them, the vast majority of early doses went to the wealthiest countries, with many offering third or even fourth booster shots to citizens when hundreds of millions of people in lower-income countries were still waiting for their first shot, particularly in Africa.

There are many complex reasons for this: while mechanisms such as COVAX were still raising funds the wealthiest governments had the resources to secure orders with manufacturers at risk, as well as investing in research and development, and scale-up, even before it was known if the vaccines would work, placing them at the front of the queue; the uncertainty around which vaccines would succeed meant many governments ordered significantly more doses than needed for their citizens; initially global manufacturing capacity was not sufficient to meet the huge global demand for these vaccines; the majority of manufacturing facilities tended to be concentrated in the wealthiest regions where political pressure could be brought to bear on supplying those countries first; and governments imposed export restrictions on both vaccines and core components and materials needed to make them, hindering the free flow of global supply. All these factors put countries with limited domestic or regional vaccine manufacturing at a severe disadvantage in terms of securing equitable and rapid access to COVID-19 vaccines, leading to significant delays.

With fewer than ten vaccine manufacturing facilities across the continent and only one locally-formulated COVID-19 vaccine (the majority of whose supply came online as demand was waning), Africa in particular has suffered the most from a lack of its own supply and development capacity. As of June 2022, 17% of people in Africa had received two doses of a COVID-19 vaccines, with 14 countries at less than 10%, compared to the global average of 60% coverage. With supply now exceeding demand, there are several contributing factors to this, including low demand, weak health systems and a lack of health care workers, but one of the reasons supply was initially limited is the lack of vaccine manufacturing facilities across Africa.

Expanding vaccine manufacturing across Africa could not only reduce reliance on imports of pandemic vaccines during a crisis, but also holds huge potential to establish regional supply lines for a wide range of essential vaccines against other infectious diseases. Not only would this benefit people in Africa, but the world over, providing a welcome boost to global vaccine production for diseases such as measles, rubella, malaria, cholera and others, while improving the health and resilience of these product markets globally.

All this has led Africa to put out an urgent call to the global community to support the expansion of African vaccine manufacturing – with the AU setting the target for Africa to manufacture 60% of its routine immunisation needs within the continent by 2040. Already more than 20 new initiatives are underway. As the world's largest purchaser of vaccines, the largest funder of vaccines for lower-income countries and the engine driving COVAX, Gavi, the Vaccine Alliance is uniquely positioned to support the realisation of this vision.

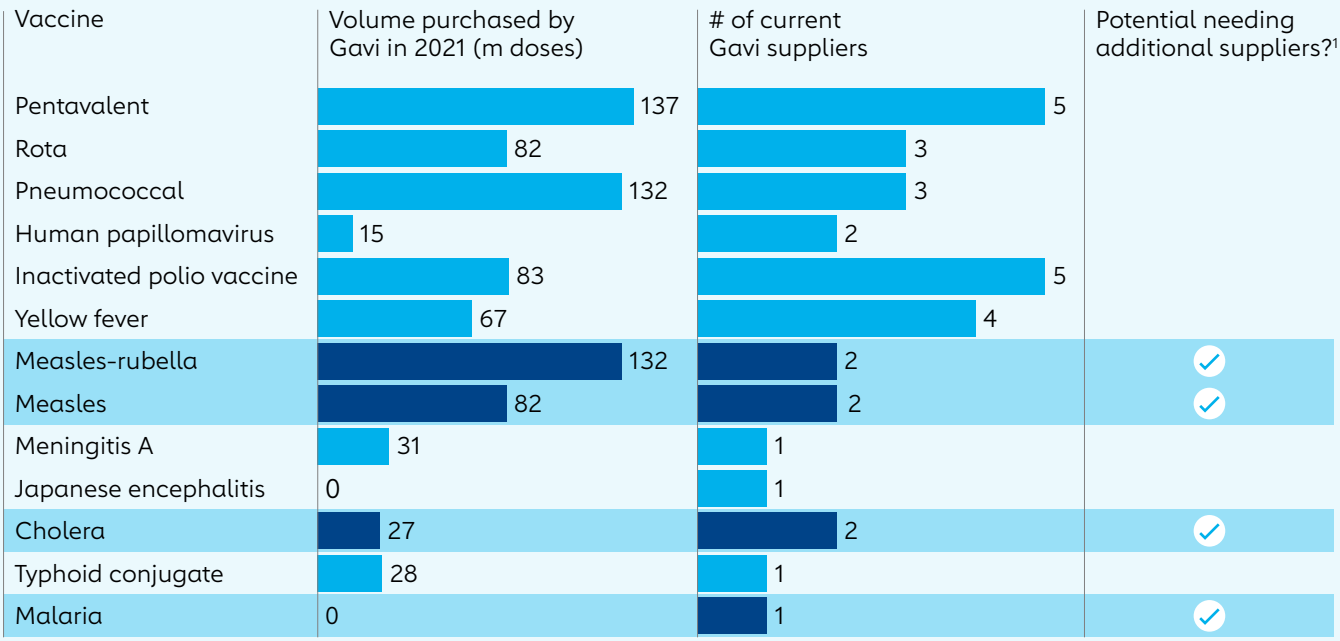
2 The opportunity

Given the delays that African nations have faced in accessing COVID-19 vaccines, the initial focus of most of these new vaccine manufacturing initiatives in Africa has been on the production of COVID-19 vaccines. The problem is not unique to COVID-19, and we appear to have been here before. During the 2009 pandemic the world's most well-resourced governments bought up almost the entire global supply of H1N1 flu vaccine, leaving the rest of the world, including African nations, to wait. Now, with COVID-19 vaccines, global supply exceeds demand and future demand for these vaccines remains highly uncertain. So, while it has been the trigger, the opportunity now is not to produce more COVID-19 doses, but rather to ensure that manufacturing facilities are in place the next time a pandemic strikes. In practice, that means having production facilities that are already up and running producing vaccines for other infectious disease, facilities that are well-staffed and producing quality products, which can then be rapidly redeployed to produce pandemic vaccines when the need arises.

There are also important practical considerations for taking this approach. Since we don't know the nature of the next pandemic threat, whether it will come from another coronavirus, influenza or another pathogen, it is impossible to know what vaccines will be needed. Therefore, building facilities that are intended solely to produce specific pandemic vaccines, and trying to keep them running between pandemics, would be neither prudent nor cost-effective. However, given the ongoing demand for vaccines used in routine immunisation programmes and vaccination campaigns against regional infectious disease, both in Africa and beyond, expanding vaccine manufacturing in Africa represents an opportunity and potential watershed moment. Not only to create much needed regional supply resilience for African nations, but also to establish Africa as a major supplier of vaccines to nations across the world.

However, for the global community to ensure success, rigorous analysis will be needed to identify the best opportunities that will most benefit people in Africa and across the world, while simultaneously helping to establish the foundations for a sustainable vaccine manufacturing base on the African continent. Initial analysis identifies several vaccine markets, where the demand volume is relatively high, but the number of suppliers is relatively low, and having additional suppliers

Figure 1 **Several Gavi vaccines would benefit from additional manufacturers to boost competition & market health**



Note: 1 Global market identified as potentially benefitting from additional suppliers (early hypothesis). Traditional/Non-Gavi supported vaccines (diphtheria tetanus, novel oral polio vaccine, BCG, hep-A) may also potentially benefit from additional suppliers/ local vaccine manufacturers

could be beneficial – including measles, rubella, cholera and malaria, and for emergency stockpiles of vaccines for diseases like yellow fever and Ebola.

The opportunity also goes well beyond existing vaccines. There are a range of infectious diseases that affect Africa, and elsewhere, for which no vaccines currently exist on the market, or for which there is a need for new vaccines. Such diseases include HIV, dengue fever, Chikungunya, Rift Valley Fever, Zika, Nipah, Lassa fever, Marburg and non-Zaire strains of Ebola, as well as pandemic influenza, adult tuberculosis and respiratory syncytial virus (RSV), many of which have been identified by the WHO as having pandemic potential and against which the development of vaccines the Coalition for Epidemic Preparedness Innovations (CEPI) is already supporting.

In addition to this, there is a need to develop vaccines with diversified and more appropriate product profiles for specific populations and cohorts. Advancements that can potentially improve usability and affordability include thermostablilty, higher efficacy, smaller packaging, and vaccines that are more tolerable and cheaper. Also, with an eye to pandemic preparedness, and the AU and PAVM's vision for supply resilience of both pandemic and routine vaccines, it may be important to ensure that the expansion of African vaccine manufacturing establishes a broad portfolio of vaccine technologies – from novel mRNA and vector-based vaccines to more traditional inactivated and sub-unit/protein vaccines – in order to help support supply resilience in Africa during the next pandemic, whatever form it takes and whatever kind of vaccine is needed to fight it.

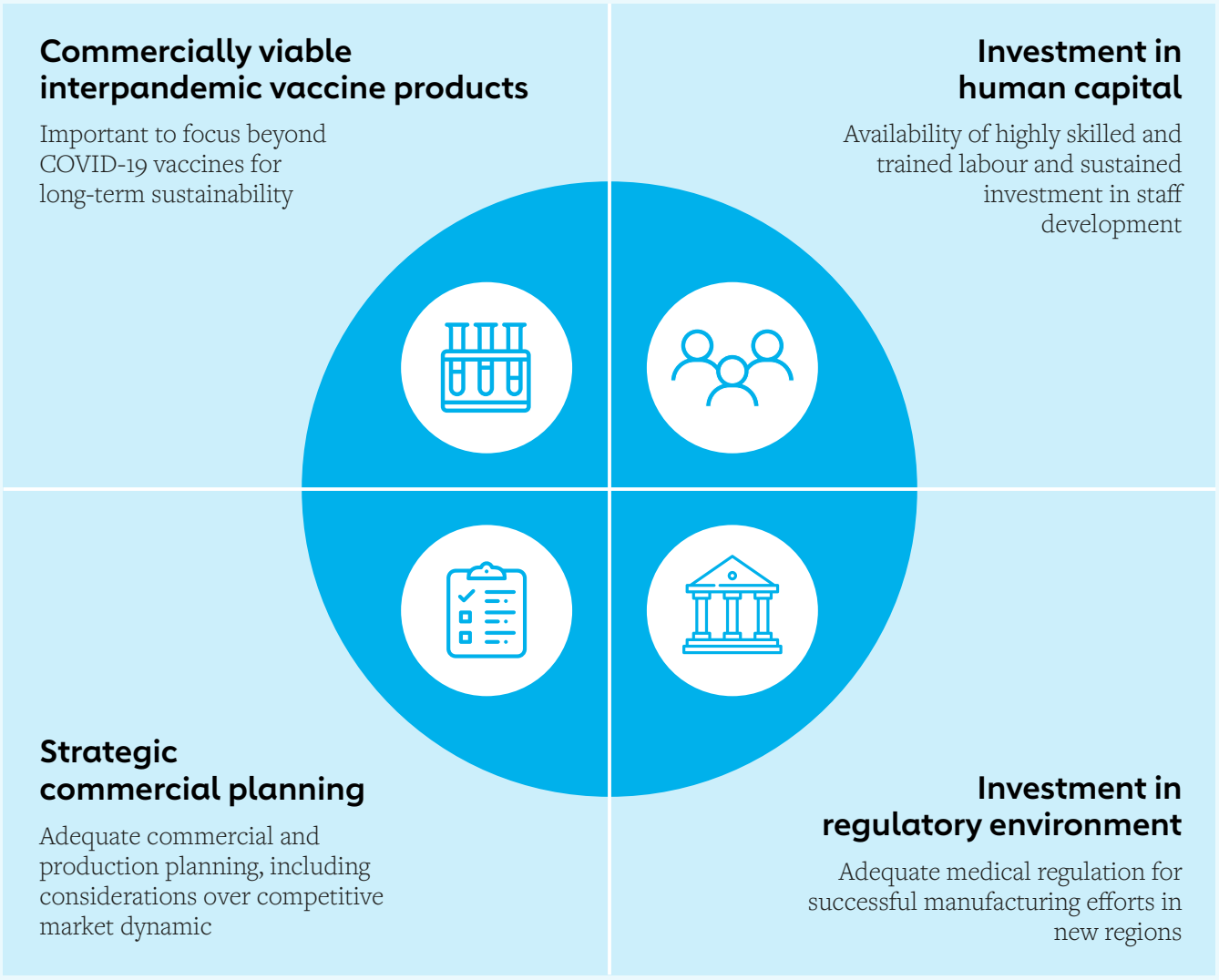
Market opportunities	Products/innovation
Existing markets where demand is high and number of manufacturers low	Measles, measles-rubella, cholera and malaria
Existing markets but with improved profiles	Enhanced thermostability, smaller packaging, lower *Cost of Goods Sold*, higher efficacy, better tolerability
Vaccines against unaddressed diseases	TB, Dengue, Chikungunya, Rift Valley Fever, Zika, Nipah, Lassa, Marburg / non-Zaire Ebola, new mRNA constructs, supra-seasonal or pandemic influenza, RSV, HIV

3 Partnership opportunity with Gavi and next steps

One of the key aims of expanding manufacturing in Africa is to create supply resilience across the continent; to enable African suppliers to help meet African demand, both at a local and regional level. As the world's largest funder of vaccines for lower-income countries, Gavi is well positioned to contribute and collaborate with the AU and stakeholders to help make this happen. Since its establishment in 2000, through its funding, procurement and delivery support, Gavi has helped vaccinate 364 million children in Africa; every year roughly 80% of children in Africa receive their basic shots through Gavi, making it a potentially important customer of African supplied vaccines for Africans.

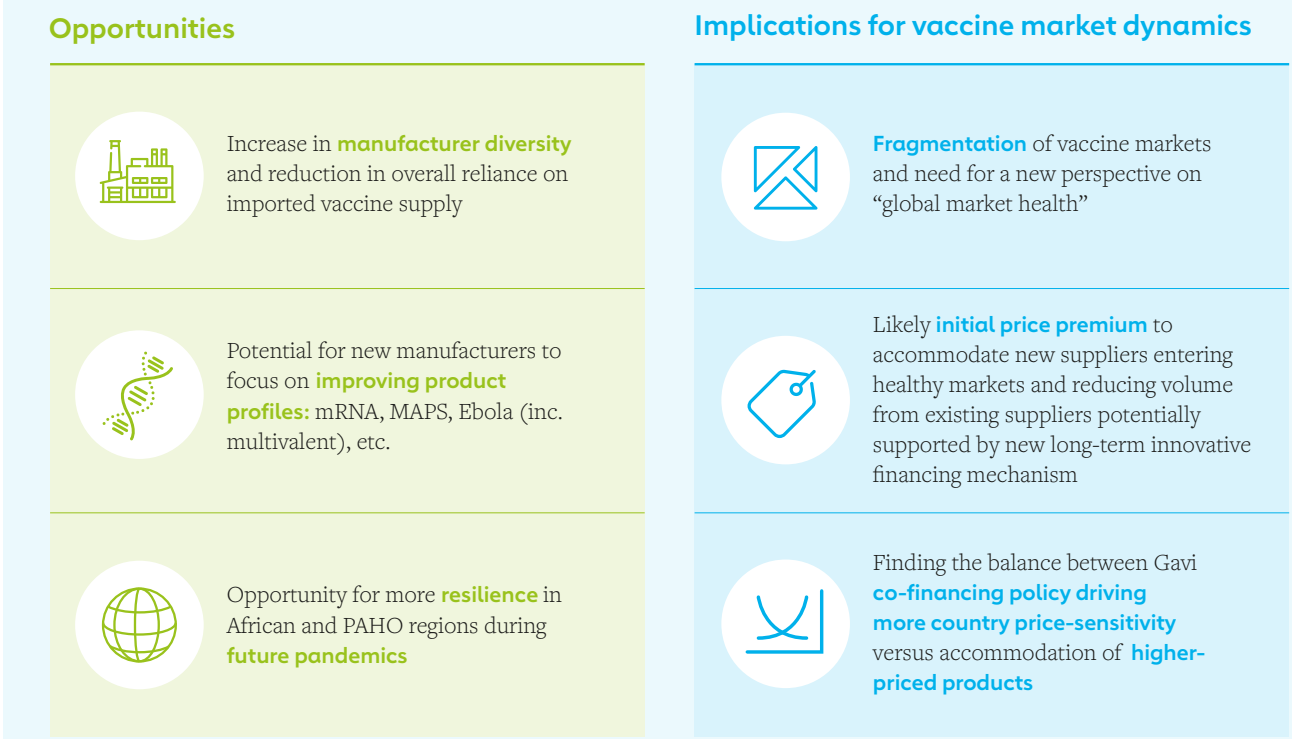
Gavi has a strong track record of contributing towards the diversification of vaccine manufacturing supply chains and improving business resilience, partnering with industry to lower demand risks by enabling and facilitating demand for new vaccines. When Gavi was first founded, its five initial suppliers in 2001 were based in Europe or North America, whereas today Gavi procures for its programmes (through UNICEF) from 18 manufacturers, only four of which are European or North American. However, as a public-private partnership, and one built on a model that includes co-financing from Gavi supported countries, an important part of its work in creating healthier markets is to increase affordability. This has significant implications for how African manufacturing might be funded.

Figure 2 **Long term sustainability for new initiatives depends upon:**



Besides the significant capital investment needed to build facilities, and the need to establish an ecosystem of expertise to support clinical research and regulatory systems, new sources of investment may also be required if this expansion is to be sustainable. Vaccine manufacturing is inherently expensive with large, fixed overhead costs, compared to drug production, with the need for highly trained skilled labour as just one significant cost driver. Bringing these costs down often involves significant challenges in reliably producing vaccine of sufficient and consistent quality, and at volume. Even multinational vaccine manufacturers can struggle with this. This is one reason why it can often take time for a new supplier to become globally competitive.

Figure 3 **Diversified regional manufacturing represent significant global opportunities**



Manufacturers of vaccines made in Africa may need to price their vaccines higher than global competitors in order to the cover the costs of starting up. That can mean that to accommodate the entry of new African vaccine suppliers, irrespective of whether that supply goes to African nations or further afield, buyers, including Gavi, and Gavi-supported countries through their co-financing portion, may initially be prepared to absorb a premium for these vaccines. In the long-term, to be sustainable and globally competitive, it will be essential for these new suppliers to produce vaccines that are attractive, both in terms of pricing and quality. In the transition period, as Gavi has helped to facilitate in other markets, long-term innovative financing mechanisms can play a role in providing enough of a 'pull' signal to build confidence for investment to take place in a sustainable manner. In recent years, Gavi-designed financing mechanisms have already helped drive additional investment and boost supply of pneumococcal, Ebola and malaria vaccines to lower-income countries. That experience will be important in helping to find the pathway to the long-term sustainability of African regional production.

Therefore, it will be important to build facilities that are capable of reliably producing high-quality vaccines that comply with globally recognised standards, such as Good Manufacturing Practice as well as Good Clinical Practice and Good Clinical Laboratory Practice. It will also be important to increase the scope and capabilities of domestic or regional regulatory bodies, such as the Africa Medicines Agency, to reach appropriate WHO maturity levels to be internationally recognised as providing stringent regulatory review, and where appropriate Emergency Use Listing during times of crisis. Setting out a reliable and harmonised stringent regulatory path across Africa will enable the acceleration and simplification of access to vaccines. Setting standards for investing in Quality Assurance and Quality Control, and having adequate bench strength to keep the regional industry globally competitive is critical.

And if the vaccines produced by these manufacturers are to be exported, regionally or globally, then such regulatory oversight, as well as quality assurance, pharmacovigilance, post-market surveillance and adverse event reporting, will also be essential.

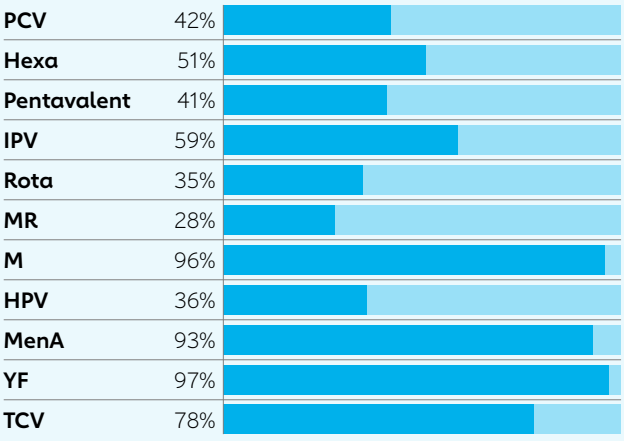
Global vaccine markets can be precarious. In anticipation of new suppliers entering a market, careful planning to help mitigate unintended consequences is needed. A new entry to a vaccine market could lead to other manufacturers reducing prices to retain their market-share, or increasing them, in anticipation of smaller orders to cover their fixed costs. Others may cut their losses and withdraw from the market entirely. In all cases this can affect the commercial sustainability of a manufacturer and have an impact on the health of the market, including pricing and availability and choice of vaccines for customers, including countries in Africa that may still be relying in part on these externally-sourced vaccines. Given its experience and anticipation of such market impacts, Gavi is committed to providing the reliable long-term demand projections and predictable long-term procurement financing for Gavi markets, which will not only give market assurances to new suppliers, but can also significantly help to mitigate potential market impacts or instabilities.

In terms of next steps for the stakeholders in the broader vaccine manufacturing ecosystem, in addition to the initial capital investment needed to build these new facilities, a well-coordinated, pan-continental plan will be essential to map out which products vaccine producers should best pursue. This will involve looking for established vaccine companies to partner with and establish technology transfers to enable rapid scale-up.

Gavi recognises that it has a core role to play as part of a partnership for a sustainable African ecosystem for vaccine manufacturing – working closely and alongside many partners, including the AU and member state governments, PAVM, the World Health Organization, CEPI and other global health bodies, donor countries, vaccine manufacturers and international financial institutions. Over the course of next six months, building on the principles set out in this white paper and working with those partners and our Board, Gavi will devise a specific plan for how it can support the sustainable entry of more African manufacturers into Gavi markets. In early Autumn, Gavi will produce more detailed analysis of the conditions required for a successful market-shaping strategy for African vaccine manufacturing. Within this, it will set out the possible roles Gavi will play, and as indicated above, where other partners, countries and agencies can act in tandem to deliver the broader ecosystem of regulatory, technical and financial support that will be required for sustainable investments. By December, Gavi will outline options for how its procurement model can best be adapted to provide some of the long-term certainty required for African vaccine manufacturers. This will include options, for consideration by Gavi's Board, for developing a long-term innovative financial mechanism within the Gavi model to provide the level of market confidence necessary to overcome initial barriers to entry and to welcome sustainable new manufacturers into specific markets.

Gavi has heard the call, by African Heads of States, for a meaningful proportion of African-made vaccines to be procured by Gavi and other global funders for both African use and beyond (Communiqué, 10 May 2022). African nations are already the recipients of the majority of Gavi-funded doses (see Figure 4). This means that Gavi's country product choice model can work in favour of new African suppliers, assuming that Gavi-supported African countries can make an early commitment that they will choose African-sourced vaccines that meet quality and value-for-money criteria as soon as they become available through Gavi. In other words, African governments – through their explicit vaccine preferences – hold one of the keys to providing investors with a credible procurement signal. As a first step in support of Africa accessing African-produced products, and to make this demand transition as seamless as possible, Gavi commits to engage with late-stage developers and manufacturers on the continent to help them understand the steps needed to have their products join the Gavi menu at the earliest opportunity, making these vaccines an option not just for African nations, but to all Gavi-supported countries.

Figure 4 **African demand as a proportion of total Gavi demand by programme** (by volume, 2025 forecast)



Conclusion

Expanding vaccine manufacturing in Africa represents a huge opportunity to improve health security across the continent. While the trigger to finally accelerate efforts to achieve this now has come from the inequitable access to COVID-19 vaccines, the need for such an expansion is overdue. Current and future generations have much to gain from improving health security through vaccine supply resilience for both pandemic threats and supply of vaccines for endemic and epidemic infectious diseases. Moreover, the ability to be ready to produce pandemic vaccines when the next crisis strikes depends upon the availability of quality and productive vaccine manufacturing capacity that is in place in order to respond. It is through the creation of that 'warm' capacity during inter-pandemic periods that a long-term industry will be built.

This represents a potentially even larger opportunity, not just to protect African citizens from a wide range of infectious diseases, but also to establish African vaccine manufacturers as important global suppliers. While the initial impetus and focus is aimed at improving health security for Africa, the ultimate goal is to build increased self-sufficiency in vaccine production. Analysis by Gavi has shown that there is need and room for more vaccine producers globally and therefore welcomes the move for Africa to become part of the solution to global access. Gavi is positioned and ready to support in the realisation of that goal, as a partner, an advisor, a future procurer and an experienced facilitator of long-term innovative financial mechanisms to create increased assurance around future demand for investors now.