In collaboration with Deloitte

WORLD ECONOMIC FORUM

Regionalized Vaccine Manufacturing Collaborative

A Framework for Enhancing Vaccine Access Through Regionalized Manufacturing Ecosystems

INSIGHT REPORT

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Foreword

Victor Dzau
National Academy of
Medicines (NAM)

Since its inception, the Regionalized Vaccine Manufacturing Collaborative (RVMC) has advocated the creation of regionally based vaccine manufacturing ecosystems. Regional systems can complement existing global networks and address the issues of inequity that came to prominence during the COVID-19 pandemic.

After more than a year of collaborative discussions and gatherings, RVMC is at an inflection point. The provisional framework we describe below presents an actionable vision to expand partnerships, bring together public and private stakeholders and build a roadmap for regions to grow production and distribution capabilities sustainably, establishing local capacities to respond at scale in times of crisis.

In launching this model, we envision the RVMC as a resource for global stakeholders, a facilitator for implementation and a connector for regions hoping to learn from ongoing efforts around the world.

Richard Hatchett
Coalition of Epidemic
Preparedness Innovations
(CEPI)

COVID-19 underscored the risks that epidemics and pandemics present to modern society while highlighting that vaccines are our most important countermeasure against such threats. Indeed, the ability to produce vaccines urgently and at scale is a foundation of society's preparedness.

In assembling the framework presented here, RVMC has consulted with dozens of subject matter experts and policy-makers from around the world. Their insight has helped us understand the complex challenges that must be navigated to establish and sustain regional capacity.

Shyam Bishen
World Economic Forum

There are many learnings from COVID 19 pandemic. The good: pandemic brought remarkable progress for development and delivery of medical countermeasures. Vaccines were developed in record time of around 10 months. The Bad: there was a lack of early access to vaccines in many parts of the world, particularly in developing countries.

This is mainly due to absence of manufacturing capacity in several regions of the world. Thus, a sustained effort to increase diversified manufacturing in the global agenda is needed to reduce reliance on a few nations or the business plans of a handful of commercial entities.

In 2022, World Economic Forum joined forces with the National Academy of Medicine and CEPI to bring about a collaboration between private and public sector to tackle this issue and help build regional manufacturing capacity. The regionalized vaccine manufacturing collaborative (RVMC) was launched during WEF annual meeting in Davos in May of 2022. RVMC has done an excellent job in consulting various stakeholders and developing this framework for diversified vaccine manufacturing which may also be applied to therapeutics and other medical countermeasures.

Greg Reh
Deloitte

Health equity starts with equitable vaccine access.

COVID-19 brought to light many inequities in the delivery of healthcare around the world. Vaccine inequity, in particular, stemmed from a lack of distributed vaccine manufacturing capacity. Deloitte has long been committed to health equity and is working with the Forum to progress the goals of the RVMC, collaborating on a framework for developing a sustainable, regional vaccine manufacturing ecosystem. Our vision of health equity is built on the conviction that no country should be without life-saving vaccines, and a strategy of vaccine production autonomy is vital to ensuring access now and in the future.

Executive Summary

The COVID-19 pandemic revealed the global community's strengths and weaknesses in responding to the most serious infectious disease outbreak of our time. International collaboration delivered safe and effective vaccines in under a year.[1] saving nearly 15 million lives.[2] Yet, many still perished, with 6.6 million confirmed deaths[3] and approximately 20 million excess deaths[4] recorded as of December 2022.

Almost a year after the first COVID-19 vaccine was approved for use, high-income countries achieved a vaccination rate twice that of lower-middle-income countries and twenty times that of lower-income countries.[5] Many factors contributed to this, but there is a clear correlation between rates of vaccine administration and regional access to vaccine development and production capacity. Africa, for example, which imports over 99% of its vaccines, was last in the queue.[6]

The Regionalized Vaccine Manufacturing Collaborative (RVMC), an initiative at the World Economic Forum, was established in May 2022. Its mandate is to help address gaps in global vaccine equity by creating sustainable regional vaccine manufacturing networks capable of producing enough vaccines for regional self-sufficiency during both normal times and when pandemics demand production surges. The framework described in this document presents regions with an economically viable pathway to that vaccine self-sufficiency and security.

The RVMC Framework assembles best practice and recommended implementation programmes that incorporate regionally relevant and actionable strategic options that can create sustainable, regional vaccine manufacturing networks. The eight pillars of the framework are designed to offer regions a way of addressing issues and opportunities. To establish regional vaccine manufacturing in a truly self-sustaining way, regions will need to work on achieving the aims of each pillar:

- **Pillar 1: Business Archetypes.** Develop sustainable commercial business operations for regionally scaled vaccine manufacturing ecosystems. Right-sizing the current global-scaled business model may reduce resource requirements by one-third and time to market by 50%.

- **Pillar 2: Healthy Markets.** Using Gavi's Healthy Markets Framework, create an efficient, unified regional vaccine market that is scaled, sustainable and transparent in routine times and during a pandemic. Regional pooled purchasing creates scale efficiencies and negotiating power for volume discounts, wider access to vaccines and a faster response to pandemics.

- **Pillar 3: Financial Models.** De-risk financing and structure an ecosystem that attracts sustained private, donor and public partnership investment throughout the life cycle of a vaccine manufacturing facility. Regional programmes generate cost benefits four times higher than investments made at a national level.

- **Pillar 4: R&D and Manufacturing Innovation.** Develop and advance regional vaccine manufacturing technology capabilities to address future pandemics. Regionalization improves access to such technologies and capabilities.

- **Pillar 5: Technology Transfer and Workforce Development.** Efficiently, effectively, and repeatably enable regions to introduce and operate right-sized vaccine manufacturing capacity at scale. To compete, regions must have incentive structures in place for retention of a qualified workforce so that vaccine manufacturers can train and deploy the local workforce.

- **Pillar 6: Supply Chain and Infrastructure.** Efficiently operate a resilient, responsive, and equitable regionalized, end-to-end vaccine manufacturing base, supply chain network and industrial infrastructure to meet normal and pandemic vaccine demand. Networked regional vaccine supply chains close to points of need among member states that are mutually dependent on one another for vaccines are much more robust and equitable.

- **Pillar 7: Product Regulation.** Enable faster access to markets for vaccine manufacturers through mutual recognition and shared submission procedures without compromising the quality, safety, or efficacy of vaccines. Harmonized regulations can accelerate access and reduce the cost of regionally manufactured vaccines.

- **Pillar 8: Policy and Governance.** Lead and implement cross-border mechanisms to raise and resolve issues fairly across a regional vaccine market. Focused leadership on regional vaccine production is needed to gather the necessary public and private cross-border agreements.

Introduction

Context

The COVID-19 pandemic revealed significant shortcomings in the global community's ability to unite for the good of humanity across national borders and ideological differences. While vaccines were developed with unprecedented rapidity and saved 15 million lives,[7] inequitable access to vaccine production and distribution was responsible for needless deaths and prolonged the acute phase of the pandemic.

Rapid COVID-19 vaccine development coupled with social measures to reduce transmission prevented much higher death tolls, but the pandemic still had extreme global impacts. As of December 2022, 6.6 million confirmed deaths[8] and 20 million excess deaths,[9] along with $14 to $28 trillion of economic damage globally,[10] were attributed to the COVID-19 outbreak.

By December 2021, one year after the first COVID vaccine was approved for use, high-income countries (>$12,000 gross national income per capita) reported double the number of doses per population than lower-middle-income countries ($1,000 to $4,000 gross national income per capita) and 20-times more than lower-income countries (<$1,000 gross national income per capita).[11] As COVID-19 vaccines were initially produced only in the United States, European Union, Russia, China and India, this inequity was directly correlated with the geographic footprint of vaccine manufacturing facilities.[12] For example, Africa, which imports over 99% of its vaccines, was last in the queue to receive them, while the United States and the European Union, which produced large quantities of vaccine domestically, secured supply agreements for enough doses to inoculate their populations many times over before distributing vaccines to other regions.

Global systems lack the flexibility to ramp up manufacturing capabilities effectively and distribute vaccines to emerging markets during global pandemics. Additionally, they lack the political authority to make rapid decisions and drive equitable allocation. COVAX was an unprecedented global coordination mechanism which raised $12.5B and distributed ~2B doses, 1.75B of which went to the 92 poorest countries. Notwithstanding its phenomenal success, the mechanism contained fatal flaws: it took too long to raise financing and vaccine deployment was delayed by export bans and other geopolitical tensions, including vaccine nationalism. This lack of equitable vaccine access underscores the need for strategic autonomy and self-reliance, anchored in distributed, regionally based vaccine manufacturing ecosystems that complement existing global systems.[13]

Countries want to have greater health security with control over vaccine manufacturing production within their borders. Unfortunately, with a few exceptions, only regions (in other words, coalitions of countries) can achieve the necessary scale of demand, investment and capability to maintain viable and sustainable vaccine production. Furthermore, new vaccine technologies (for example, mRNA and other 'programmable vaccine' approaches) that were proven during the response to COVID-19 offer breakthrough opportunities to improve pandemic preparedness and health. Effective regions can speed up the acceptance and application of these revolutionary programmable vaccine technologies across country borders to control the spread of neglected and new infectious disease vectors and outbreaks.[14]

Regionalized Vaccine Manufacturing Collaborative (RVMC)

RVMC is an initiative at the World Economic Forum that aims to reduce the gaps in global vaccine equity and enhance access to vaccines for all populations. It will achieve this by establishing sustainable regional vaccine manufacturing networks capable of producing enough vaccines for regional self-sufficiency during both normal times and when pandemics demand production surges.

Launched at the Forum's Annual Meeting in Davos in May 2022, RVMC is co-chaired by the Coalition for Epidemic Preparedness Innovations (CEPI) and the US National Academy of Medicine. Steering committee members include leaders from the Africa Centers for Disease Control and Prevention, Aspen Pharmacare, Biological E, Developing Countries Vaccine Manufacturers Network, Gavi the Vaccine Alliance, Global Health Innovation Technology Fund, International Finance Corporation, Ministry of Foreign Affairs in Norway, Ministry of Health in Singapore, Ministry of Health in Indonesia, Ministry of Health in Brazil, Moderna, Pan American Health Organization, US State Department's Bureau for Global Health Security and Diplomacy, World Trade Organization, World Health Organization and Wellcome Trust.

RVMC has worked to identify opportunities to accelerate ongoing regional capacity-building efforts, build political support for regionalization, promote regional cross-learning, link regional efforts to global fora and initiatives (such as the G7, G20, African Union and Johannesburg Process), and document leading practices that increase vaccine manufacturing capacity, improve equitable access and respond to pandemic and routine needs. The result of a year of multilateral discussions is the RVMC Framework: an end-to-end approach for establishing self-sustaining regional vaccine manufacturing ecosystems.

By using this framework, regions can assess their status and leverage best practice to create action plans for effectively and efficiently implementing regional initiatives.

RVMC Framework Overview

Defining Regional Initiatives

Regional coalitions that bring together nations with similar disease targets, health needs and governance priorities will benefit from coordinating a cross-border vaccine manufacturing ecosystem. Creating a common regional vaccine market by pooling demand and manufacturing capacity enables regional initiatives to achieve a scale that would otherwise be unattainable. Effectively functioning regions also minimize the time and complexities of decision-making, and deliver faster responses to health emergencies, such as pandemics. The size, complexity and scope of regional initiatives will vary according to the needs of their member countries. Any of the pillars in the framework can serve as a starting point to kickstart regional initiatives.

Benefits of Regional Vaccine Manufacturing Ecosystems

Global vaccine manufacturers benefit from economies of scale by concentrating production in a few locations with well-developed infrastructure. However, this model can contribute to inequality and create supply chains that are susceptible to single-point-of-failure disruption, as seen during recent pandemics for Mpox and COVID.

Conversely, local, country-specific manufacturing can provide increased flexibility, faster speed to market, lower vaccination hesitancy and greater resilience, but few countries acting alone can support a complete vaccine manufacturing ecosystem that can compete against a global model.

This document outlines best practice for applying the framework to support the expansion of competitive, local vaccine manufacturing capacity. It shows that it's possible to pool markets supplied by regional supply chains and right-sized manufacturing technologies and maintain a responsiveness and flexibility that's not possible in global operations.

World Bank analysis[17] shows that regional investment in vaccine manufacturing, R&D and regulation capacity building will cost less than 1% of total government health expenditure while returning cost-benefit ratios four times higher than national-level investments. Collaborative regional governance can improve access to technology, financing, and markets to enable sustainable increases in vaccine manufacturing.

Eight Pillars of the RVMC Framework

The eight pillars of the framework are the building blocks of a regional ecosystem, designed to show regions how to address the issues and opportunities they may face. To establish regional

vaccine manufacturing in a truly self-sustaining way, regions will need to work on achieving the aims of all these pillars:

Implementation of the pillars must be synchronized and adapted to regional needs and ambitions. Regionally contextualized roadmaps will need to focus on economic sustainability and innovation to ensure equity. As regions execute against their roadmaps and advance along their respective journeys towards maturity, they can also apply the lessons learned for vaccine manufacturing to other industries, turning regional self-sufficiency for pandemic response into more general and truly sustainable economic development.

Pillar 1: Business Archetypes	Develop sustainable commercial and public sector business operations for regionally scaled vaccine manufacturing ecosystems.
Pillar 2: Healthy Markets	Using Gavi's Healthy Markets Framework, create incentives to direct the flow of capital toward regional manufacturing capacity and achieve an efficient, unified regional market that is scaled, sustainable and transparent in both routine times and during a pandemic.
Pillar 3: Financial Models	De-risk financing and structure an ecosystem that attracts sustained private, donor and public partnership investment throughout the life cycle of a vaccine manufacturing facility.
Pillar 4: R&D and Manufacturing Innovation	Manage the portfolio of basic, clinical, and applied manufacturing and translational research required to integrate processes, continuously improve yields, assure quality, and promote innovation to achieve the regional vaccine platform coverage, scale, compliance, and optimization necessary to be competitive.
Pillar 5: Technology Transfer and Workforce Development	Efficiently, effectively, and repeatably enable regions to introduce and operate right-sized vaccine manufacturing capacity at scale. To compete, regions must have incentive structures in place for retention of a qualified workforce so that vaccine manufacturers can train and deploy the local workforce.
Pillar 6: Supply Chain and Infrastructure	Efficiently operate a resilient, responsive, and equitable regionalized, end-to-end vaccine manufacturing and supply chain ecosystem to meet normal and pandemic vaccine demand.
Pillar 7: Product Regulation	Enable faster access to markets for vaccine manufacturers through mutual recognition and shared submission procedures without compromising quality, safety, or efficacy of vaccines.
Pillar 8: Policy and Governance	Lead and implement cross-border mechanisms to address challenges and opportunities through a collaborative regional policy framework.

FIGURE 1 | **Eight Pillar RVMC Framework**

Pillar 1

Business Archetypes

One of the big lessons learned during the COVID response was that vaccine production is scaled and configured for either global or national supply chains. Therefore, to establish regional production, current business models must be right-sized. Manufacturers must achieve a minimal viable regional production to manage the trade-off between agility and scale that resulted in inequitable vaccine access during the response to COVID.

This section puts forward options that address these issues, enabling regions to configure vaccine manufacturing and right-size operations for their markets.

Path to Implementation

Step 1: Select Business Archetype and Positioning Strategy

To date, the biopharma industry has employed an architecture that capitalizes on low-cost, globally scaled manufacturing and supply-chain models. IFC scenario-modelling studies[17] suggest that right-sized regional models can be established at costs between two and five-times lower than – and at twice the speed of – global models, while accessing regional markets can return three to six times more than fragmented country markets can today.

Choosing a core manufacturing business archetype provides a starting point to right-size operations. Regions should evaluate the feasibility of each option, including commissioning new vaccine and bioprocessing facilities or expanding existing ones, and positioning themselves to improve upon or expand traditional operations.

A region should support a diverse set of business archetypes (listed in Table 1 below). This helps them overcome any disadvantages of pursuing a single archetype and enables them to address specific market needs effectively, maximizing their competitiveness. Once chosen, the archetype employed is not fixed: the configuration can evolve in accordance with the business's roadmap, shifting technology, markets, and competitors' landscapes.

TABLE 1 **Business Archetypes for Select Capabilities and Functions**

Archetype	Role	Strategic Advantages
CMOs (Contract manufacturing organizations)	Producers act as contractors and synthesize vaccines developed by larger pharmaceutical firms who provide the IP and protocols for a set cost.	Low-cost manufacturing and workforce, and direct control over manufacturing and quality operations. It avoids R&D, clinical trials and B2C marketing expenses.
CDMOs (Contract development manufacturing organizations)	As CMO, plus limited late-stage development research capabilities, such as developing second-generation products or being contracted for R&D tasks by larger pharmaceutical firms. Can include revenue sharing.	Access to clinical patient populations for more efficient clinical trials and regulatory approvals. May offer preferential access to regional markets.
Locally/Regionally focused biopharma	Concentrate on developing and commercializing niche vaccines or ingredients to address specific diseases and priorities of regional markets.	By targeting regional patient populations and avoiding entrenched competitors, specialty biopharma companies can achieve profitability even with lower manufacturing volumes.
Biosimilars	Companies can specialize in biosimilars at lower costs than existing branded vaccines. Companies can obtain licenses from NIH or similar agencies and further develop vaccines to commercialization.	Avoids marketing and R&D costs and leverages established processes, low-cost scaled supply chains and reduced regulatory burdens.
Ancillary products and services	Produces raw materials, excipients and adjuvants with locally sourced and more secure and responsive supply chains.	High enough demand for regionally sourced raw materials to command privileged access to markets.

Note that although the archetypes above focus on minimizing capital requirements to establish a minimum viable business, there are also relatively straightforward ways of using public sector support to secure end-to-end capabilities, such as Fiocruz, and state-owned enterprises. Furthermore, established, individual manufacturers may decide to offer combinations and hybrids of the archetypes in Table 1 that are tuned to regional requirements to create sustainable competitive advantage.

Step 2: Assemble, Test and Scale Minimum Viable Business

The minimum viable business is designed to come to market as quickly as possible with the minimum amount of investment. It offers a basic version of operations that can be added to, adapted and improved upon in the future after model viability is confirmed and competitive and market response is understood. To launch the minimum viable business, regions must:

1. **Select critical business archetype components.** Once a manufacturer selects a viable core manufacturing archetype, they must select which of the critical business components to make, buy or secure via partnership. Considerations for business archetype components include how personnel, processes, tools and technologies function, and synchronize to consistently achieve key operating metrics and goals.

2. **Right size each component.** Simply hiring an experienced person who has managed the function at a global or country level is likely to be insufficient – these critical personnel must be supported to scale processes and technologies to fit the new regional operating model.

3. **Integrate components into the core.** Assess the ability of each component to fulfill the minimum requirements both individually and in combination. Carry out and learn from assessments of the critical components necessary to supplement the core manufacturing archetypes, then roll out. As a first step, regions can conduct a comprehensive regional feasibility assessment of any proposed manufacturing technologies, local capabilities, market dynamics, funding sources and partnerships to ensure each business component is viable.

Note: Regional public and private sectors need to coordinate their activities. The regional public sector plays a critical role by first creating an environment for success as the primary customer for much of the production. The private sector can then build a portfolio of manufacturing archetypes from among the most economically sustainable options while ensuring equitable and affordable regional access to vaccines. The portfolio should include a variety of business archetypes to ensure a healthy balance of competition and differentiation.

Pillar 2

Healthy Regional Markets

Regional markets offer advantages to:

- **Member nations:** Regionally aggregated demand across member states creates scale efficiencies, improves negotiating power for volume discounts, establishes certainty of demand, simplifies and scales procurement and transactions, and enhances equitable distribution during both pandemic and routine times.
- **Manufacturers:** Right-sized manufacturing facilities producing regionally approved, identically specified products and labels across national borders can significantly lower manufacturing costs and reduce regulatory risks. Predictable, sustained baseline demand from regions deploying advanced purchasing and capacity reservation agreements also improves the planning and economics of ongoing plant operations.
- **Public Health:** Regional markets can also offer a more effective and faster health system response to infectious diseases that spread beyond country borders. Single-market product approvals enable national immunization programmes (NIPs) to be synchronized across member states and facilitate the integration of information throughout the region, improving flexibility, equity and coordinated pandemic preparedness and response.
- **Innovation:** Regions can also create sufficient demand to profitably develop and manufacture vaccines for neglected diseases, improving IP protection and innovation.

Nations can either join an existing common market or facilitate the creation of a new market with partner nations.[15]

Path to Implementation

Step 1: Aggregate Demand

To form a common cross-border regional market for vaccine products, countries, suppliers and buyers will need to take several steps:

- **Build a coalition** by identifying potential partner countries with a shared interest in assembling a regional initiative. Examples of common ground can include similar health systems, disease prevalence and vaccine needs, and aligned legal or regulatory systems. Geographic proximity can also help but is not the only consideration in selecting member state partners. Once potential partners come together, diplomatic leadership and regional champions in all members states must be empowered to work across borders. They will need to gauge and align interests into a vision, objectives, roles and decision-making processes that can be clearly articulated.
- **Select vaccine portfolio, aggregate vaccine demand and generate forecasts** for diseases of regional interest, desired health outcomes and the technologies to be explored – CEPI, Gavi, and WHO can offer a starting point for this work. Most critically, regional markets can stipulate a set of product specifications, claims and labels that provide several countries with access to a single vaccine product. Based on the selected portfolio, calculate the combined current bounded vaccine demand of all participating countries, work out the unbounded potential demand for the current vaccine programmes and forecast the planned future demand for the member countries. Aggregated forecasts enable regions to offer a scaled, more predictable demand that can attract better-qualified vaccine suppliers, negotiate lower prices and priority access over longer periods, and form the basis for advanced purchase agreements and improved equity.
- **Qualify suppliers, coordinate and pool financing and procurement** for streamlined and bulk purchasing of target vaccines. Based on the vaccine products they select for their marketplace, regions can develop a funding mechanism for procuring vaccines and managing tenders. This can involve pooling financial resources from participating countries, seeking support from international organizations and accessing regional development funds. Regions can design and implement the market's tender pre-buying, purchase and post-buying quality, safety and procurement monitoring processes. Member states can also share supplier information, negotiate and centralize group contracting, and establish cross-border e-marketplaces with transparent operations.

In addition, regions can define and maintain consistent product specifications and labels to be made available across the regional common market, avoiding the high cost of complex and fragmented product offerings. The African Vaccine Acquisition Trust initiative[15] and the PAHO Revolving Fund are good examples of regional, pooled procurement mechanisms. See pillars three (Financing Models) and six (Supply Chain and Infrastructure) for more details.

Step 2: Attract Supply

Regions must attract multiple vaccine suppliers to compete in the marketplace and ensure supply security. A single supplier with a monopoly can lead to price gouging. For manufacturing-scale economy, it may be more pertinent to have one supplier of each different product within a region. At the same time, too many suppliers can fragment scale and increase the cost of transactions, products and product handling. Initially, regions may wish to consider inviting three to five manufacturers to supply the market and adapt that number as needed. Regions can reduce the risk of relying on single sources for critical vaccines while improving access to suppliers that address neglected, new and outbreak diseases by operating multi-source procurement programmes that:

- **Actively solicit information and tenders from alternative suppliers** and invite them to participate in transparent selection processes. This will build diversified capacity within the region and hedge against single points of failure.
- **Develop transparent, objective vendor qualification programmes** to evaluate, qualify and select potential vaccine manufacturers to supply the market.
- **Promote market competition** among vaccine manufacturers to enhance quality, supply and affordability. Encouraging technology transfer can establish new sources of local vaccine supply and fill product gaps, while creating regional market-oversight authorities can protect against and resolve anti-competitive behaviours.
- **Require uniform product specs and labeling.** Avoid single manufacturers cornering national markets by stipulating that identical products, claims and labels must be available to all countries participating in the regional marketplace. This prevents tiering and ensures scaled, equitable product access.
- **Utilize regional supply infrastructure.** Unified markets must define standard service levels and requirements for manufacturers to import, transport, store and distribute their products consistently. This helps limit the potential of manufacturers cornering markets and ensures quality and equitable availability of vaccines.
- **Obtain sustainable public/private procurement financing.** Long-term purchase agreements in large regional markets de-risk capacity-expansion investments for new suppliers and expand access to vaccines. These mechanisms can also be deployed to support vaccine research, development and production, encouraging a diverse range of supply sources that can eliminate pinch points in regional supply chains. See pillar three, Financial Models, for more.

Step 3: Build and Shape Healthy Markets based on Gavi's Healthy Markets Framework

Gavi's Healthy Markets Framework was designed to shape LMIC vaccine markets, predominantly in Africa. Regions can expand, tailor and apply Healthy Markets Framework principles based on their needs and goals. To establish regional common markets, regions can:

- **Eliminate trade barriers**, including tariffs, quotas and non-tariff barriers that hinder the free movement of vaccines, personnel, data and capital across the region.
- **Create regulatory pathways to accelerate entry to market**, minimizing time lags between submission, review, approval and product access and reducing the variability of vaccine product specifications in a regional market. See pillars seven and eight, Product Regulations and Governance, for more.
- **Drive and maintain healthy, predictable pooled demand** that's aligned with the health policies, disease monitoring and pandemic response plans of member states across the common market. Vaccine demand forecasts, stockpile levels and capacity should be made public.
- **Establish transparent procurement operations to secure an equitable and reliable supply.** After qualifying suppliers (see above), buyers, including governments, donors and international organizations, can make objective, evidence-based decisions during regional vaccine selection processes, establish equitable vaccine procurement, digitally automate transaction and payment procedures, and publicly disclose contracts and prices.
- **Negotiate sustainable and competitive pricing.** Healthy Markets Framework pricing considers manufacturing costs, R&D investment, member states' preferences for vaccine products, regulations and the public health impact of vaccines. Surge capacity programmes to improve responsiveness during disease outbreaks must be supported directly through Healthy Markets Framework pricing. This should be achieved through price supplements to make surge capacity requirements affordable during outbreaks.
- **Share healthy market information.** Feed real-time demand data from member-state health systems into supplier demand forecasting and sales and operations planning systems. This increases market efficiency and enables manufacturers to optimize production runs, improve inventory management and manage supply chains more effectively. As a result, producers can reduce overall costs, fund outbreak surge capacity and enhance the availability and equitable distribution of vaccines across the common market. See pillar six, Supply Chain and Infrastructure, for more.
- **Promote public awareness and education** on the importance of vaccination, vaccine safety and product benefits across the marketplace to stimulate demand in target populations and overcome vaccination hesitancy. Public advocacy campaigns build trust, generate consistent market demand, and encourage vaccine uptake.

Step 4: Optimize and Sustain Regional Markets

Once common regional vaccine markets are developed, they must be optimized over the long-term to achieve a diversified supplier landscape, build a regionally pertinent vaccine R&D portfolio, stimulate innovation and balance economic sustainability with production scale. Market-shaping activities incorporating these factors must be applied carefully to avoid anti-competitive behaviour. While global agencies often have a fixed vaccine portfolio, such as Gavi's Vaccine Investment Strategy, regional initiatives might consider strategies like designing their vaccine portfolio based on prioritizing regional pathogen and vaccine needs. This would ensure crucial supply security, complementarity and coverage for regionally pertinent vaccines while avoiding unnecessary competition and creating a healthy, common, regional market.

Regions must develop roadmaps, deploy market-shaping tools, iteratively refine forecasting, and optimize market-shaping programmes over time. The following gives some idea of how to go about this.

1. **Develop market-shaping roadmaps**

– **Develop a regional production goal:** This may be similar to PAVM's goal of producing 60% of the vaccines Africa needs locally.[16]

– **Create demand projections:** Robust demand forecasts over a 5- to 10-year horizon for Gavi and global markets should be based on public health needs and purchase preferences.

– **Plan supply capacities:** Production capacity planning should be tightly coordinated to respond to short-term fluctuations but flexible enough to accommodate long-term demand forecasts.

– **Achieve target supply-and-demand balance:** Based on the specified target supply-and-demand balance, regions can take active measures to shape the market and protect against deviations from the target pathway.

2. **Deploy market-shaping toolsets to increase equitable market access.** Some of these tools include:

– **Advanced purchase and capacity reservation agreements** which increase the predictability of supply and de-risk manufacturing capacity expansion projects.

– **Bespoke vaccine modifications** that give products characteristics which reduce projected supply-and-demand imbalances. For example, single dose, improved duration, lower adverse events, improved shelf life or Halal formulation.

– **Incentivized surge capacity build-out.** For some diseases, 20% to 30% additional capacity will be needed to protect unvaccinated populations during outbreaks. The price increases required to bring additional capacity onstream during outbreaks often result in inequitable access to vaccines.

– **Long-term purchase agreements.** By extending advanced purchasing horizons, competing suppliers can gain access to future expanded markets.

– **Differential or tiered pricing models** can be utilized based on a member's economic capacity and health needs. This balances equitable access with manufacturer financial requirements, but tiered pricing must be transparent and maintain consistent quality standards.

– **Vaccine allocation frameworks** to ensure target populations are equitably served in times of constrained supply. Critical for outbreak and pandemic situations, as well as for enhancing coverage for routine immunization.

3. **Optimize and actively monitor the markets, making course adjustments as needed.**

In time, RVMC regional markets can improve supply-and-demand forecasting accuracy and granularity and lengthen forecasting time horizons by:

– Applying directed market monitoring programmes to proactively manage risk and better time the deployment of market-shaping tools.

– Conducting surveys, for example, of epidemiology, suppliers or health, to supplement forecasting datasets.

– Collecting more comprehensive real-time data about supply (such as from vaccine manufacturers and the supply chain) and demand (such as from the health system or disease surveillance).

– Developing advanced AI, automated expert and decision support systems, and machine learning analytical and data visualization tools to run scenarios and continuously update forecasts.

Single, unified, regional markets can generate the scale required to support RVMC manufacturing capacity expansion. These markets are enabled by financing and regulations that establish the rules of the road' and unified product specifications that support the vaccine healthcare demands of each member state.

Pillar 3

Financial Models

Funding for vaccine manufacturing capacity exists across a variety of public, private and donor organizations. Furthermore, according to a recent report published by the International Finance Corporation, the benefit-cost ratio of proposed projects increases by up to six times when delivered regionally rather than for individual nation markets.[17] This suggests that nationally proposed vaccine manufacturing projects that appear only marginally economical or even unprofitable in a feasibility study can become profitable when they're set in a larger regional market.

The remainder of this section outlines the feasibility studies and de-risking options that financiers require to deploy funds. This information helps manufacturers implement business plans that lower the costs of capital and make projects economically attractive to alternative funding sources, allowing investors to consider repeatable, scalable financing opportunities that extend beyond country borders, and regional leaders to organize stakeholders, policies and infrastructure, health and social programmes that enable them to benefit from participation.

Path to Implementation

Step 1: Conduct Project Feasibility Studies

As a first step to expanding regional vaccine manufacturing capacities, financiers will need a comprehensive set of feasibility studies to evaluate any funding request they receive. Third-party validation by experts (for example, in bioengineering or regulation) with proven experience and credibility is essential for any investment, and such due diligence will strengthen the business case for investors who hold fiduciary responsibility for ensuring they've quantified the risks of any bankable projects. Since proposed projects may have drastically different financing needs based on regional maturity, required technology and production location, regions should create a systematic method for evaluating a wide variety of vaccine manufacturing projects.

For more, see the Unabridged RVMC Framework for feasibility studies.

Step 2: De-risk Financial Returns

Private financial institutions will seek to eliminate, transfer, mitigate or manage each investment risk identified through the feasibility studies covered in step 1. To prepare for discussions with these institutions, manufacturers can use risk matrices to help them identify the areas likely to be of greatest sensitivity to financiers. By systematically understanding the de-risking priorities of financiers, manufacturers can adjust their implementation plans and capex and opex budgets and actively manage fund solicitation and deployment in a way that optimizes the cost of capital and funding sources for RVMC projects. As a consequence, lead investors can efficiently mobilize funding partners and fine-tune the timing and scope of investments, and regions can direct public and private partner involvement and contributions.

Public-private partnerships (PPP) can enable rapid development by pooling capital for resource purchase and asset development. By combining the two investment streams, regions can access the benefits of both funders simultaneously and balance private sector discipline and cash-flow flexibility with public-benefit outcomes. PPPs evolve over time, with heavy initial public investment tapering into smaller, supporting incentives as process technology and financial instruments mature. This model is particularly useful in funding infrastructure projects that ensure equitable vaccine access in resource-constrained areas using public bond raises. Public and donor support helps de-risk private financing, make projects more viable and improve the path to profitability, especially by lowering the financial burden for operators through grants or longer-term loans.

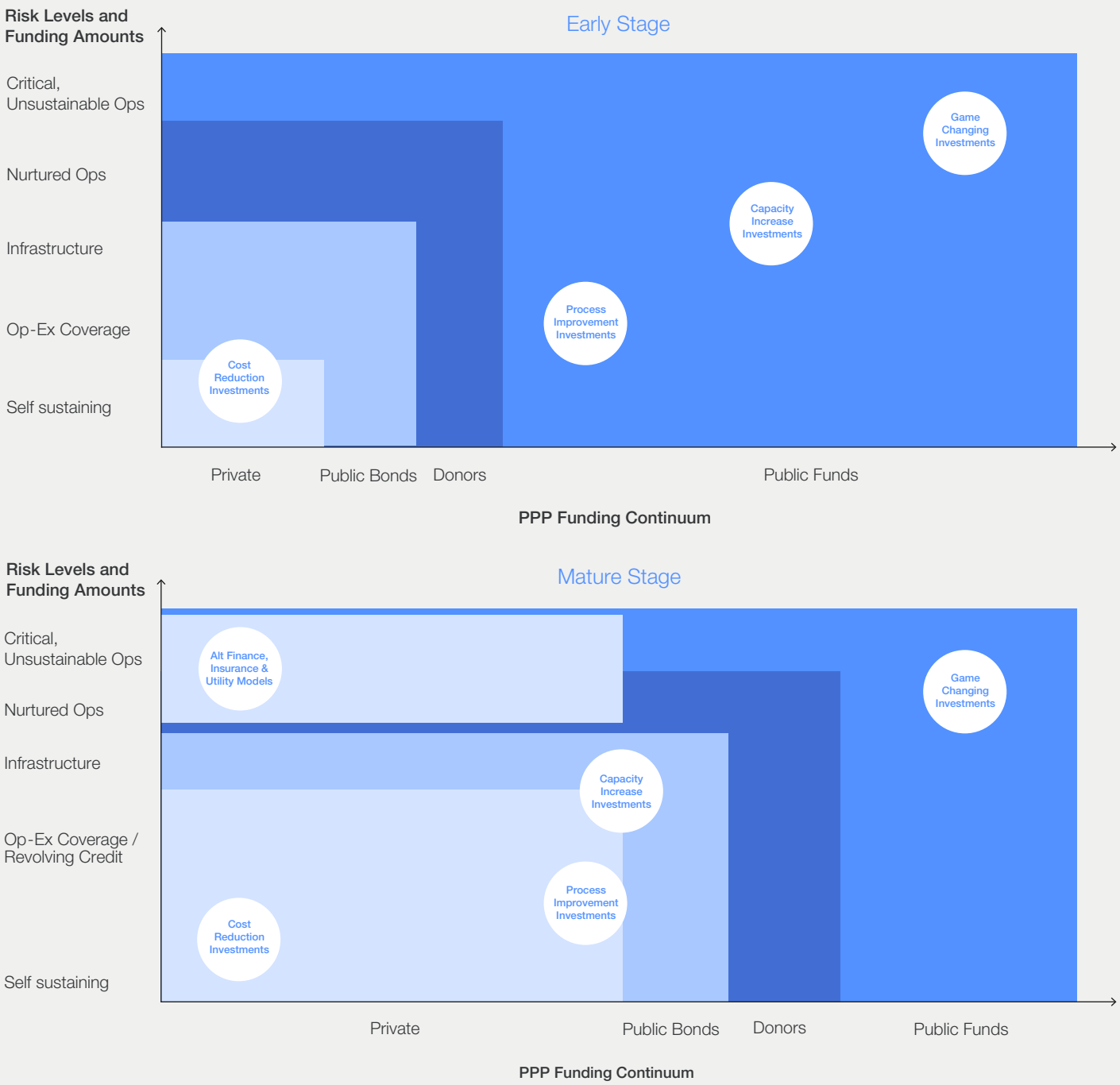
For more, see the Unabridged RVMC Framework for de-risking approaches.

Step 3: Develop Targeted Financial Instruments

Regardless of the composition and maturity of the funding ecosystem, different technologies and business models have a range of financing needs. A winning long-term strategy will ensure that a variety of financial instruments are in place to create resilient, equitable and diverse regional vaccine manufacturing ecosystems and markets. Regional entities and NGOs can work with private financiers to backstop specialized instruments to make private funding for bankable vaccine manufacturing possible earlier. Innovative financial instruments can be developed to incentivize both public and private sector participation. See Unabridged RVMC Framework for a representative portfolio of instruments for consideration.

Figure 2 below illustrates how the distribution of funding sources across the PPP continuum is initially heavily dependent on public funds during facility build out and advanced purchase agreements. As the manufacturing facility achieves commercially scaled operations and generates sales, financing transitions to a blend of private funds, public bonds, and donors. Funding coordination can be led by a specially convened consortium of regional leaders drawn from each sphere. This should avoid duplication and help encourage complementary investments.

FIGURE 2 **Evolution of risk levels, funding amounts and key players as financing models progress from early to later stages**



Pillar 4

R&D and Manufacturing Innovation

This pillar explains how regions can innovate and continuously improve vaccine manufacturing technologies to always respond effectively to infectious diseases. Without such innovation, over time, competitors from outside the region will enter with lower costs and better products, displacing regional production capacity. Even biosimilar vaccines need innovation to keep costs down, improve yields and qualify new supply sources. Regional programmes must manage a portfolio of potential major and incremental improvements that address regional diseases of concern. Access to innovation is a critical component of any proposed project.

Path to Implementation

Step 1: Establish Regional Vaccine Manufacturing Innovation Strategy

To develop and sustain a regional vaccine manufacturing R&D strategy, regions can foster a collaborative innovation ecosystem that coordinates the activities of regional expert teams, identifies R&D opportunities and gaps, convenes and develops regional expert resources and pools critical resources. Regions can aggregate fragmented member-state data and enable a regional data-sharing infrastructure that supports public health experts, epidemiologists, manufacturers, healthcare professionals and research scientists to collaborate on research activities (see Unabridged RVMC Framework for more information).

Once the enabling conditions for regional expert collaboration on innovation programmes are in place, regions can invest in targeted basic, clinical and applied research programmes with a higher likelihood of success. A region that selects a technology and then focuses on applied research and works back to riskier clinical and basic research can have an advantage and earn returns faster with less risk – especially if it invests in vaccine manufacturing platform expertise, scaled-up manufacturing facilities and regulatory capabilities. The ‘applied to clinical to discovery’ research roadmap defined below is the reverse of the path vaccine programmes traditionally take, but new regions will find it hard to catch-up if they follow the path of international teams with a 20-year head start in basic and clinical research.

1. **Applied and Translational Innovation Programmes**

Selection of the most appropriate vaccine manufacturing platform technologies depends on regional capabilities, ambitions and the nature of the target disease. Whole virus and new programmable vaccine technology platforms are viable applied research manufacturing platforms.

There is insufficient applied vaccine manufacturing research globally, so new regions willing to invest in scaling up and developing GMP-validated facilities to train operators, test, right-size and optimize the components of production, such as cell culture, bioreactors, purification, formulation pack-out and manufacturing quality assurance and control operations that can fully exploit a region’s selected technologies, can find themselves on an equal footing with established programmes around the world.

The cut of platform technology leads to dramatic differences in the capital investment, technical expertise and timelines required, as well as the success rates that can be achieved. Accordingly, this pillar promotes the diversification of R&D and manufacturing to make it easier to select the most appropriate vaccine.

The mRNA COVID vaccines demonstrated that programmable vaccines have exciting new potential and may speed new vaccines to market more safely, at scale, at lower costs and with greater operational flexibility than attenuated and whole virus platforms. There may be an opportunity for regions to address diseases of neglect and unmet medical needs in new ways, using directed research programmes to leapfrog older technologies. For each disease and region, the playing field may be more level in new technology spaces than it is in established technology. A regional portfolio of both traditional and programmable technologies can address more pathogens, diversify risks, create resilience and optimize health outcomes.

See the Unabridged RVMC Framework for a list of applied and translational vaccine manufacturing research opportunities.

2. Clinical Development Programmes

Focused and selective regional clinical research can supplement applied and translational innovation programmes and support pandemic preparedness and response plans. Initially, regions can standardize regulatory data management and regional submission-supporting post-market surveillance and safety to manage outbreaks or adverse events for approved, marketed vaccines. Regions may need to conduct regional clinical trials to develop novel, safe and effective vaccines for diseases of neglect, advance regional formulation preferences and focus on targeted populations. Start by supporting existing studies and pipelines, and work with state, regional and global regulators to improve trial design, study execution and site management of study data to facilitate regional product approvals. Ultimately, regions can develop their own networks of clinical investigators and good clinical practice facilities to provide equitable access, recruit target patient populations, conduct clinical studies and distribute vaccines for targeted regional diseases and vaccine development programmes. Critical for success is ensuring that regional and member-state regulatory maturity level programmes build the necessary capabilities and capacities as they expand their clinical development.

See the Unabridged RVMC Framework for descriptions of clinical development opportunities for regions.

3. Discovery or Basic Research Programmes

Finally, regions may require selective discovery research programmes. Regions have preferential access to unique disease vectors of global research interest that local researchers can leverage. Access to super-computer design and high-throughput screening facilities can accelerate the detection and optimization of vaccine leads. Independent and university labs can conduct much of the basic research, but preclinical submissions will require some tests to be conducted under good laboratory practice conditions that typically require a manufacturer or contract research partner, and preclinical in vivo studies require a vivarium. The timeline from discovery to marketed vaccine product is typically 10 years.

See the Unabridged RVMC Framework for descriptions of basic research opportunities for vaccine manufacturing regions.

Step 2: Prioritize and Resource a Portfolio of Technologies

Regional expert teams can use frameworks based on data and risk-reward criteria to manage technology portfolios and decide upon and budget for regional vaccine manufacturing innovation initiatives. For sustainability and to manage innovation risks, a major manufacturing region will require a diversified portfolio of R&D programmes and projects that runs across the full spectrum of applied, clinical and basic research. The pathway to a diversified portfolio will be unique to every region, based on starting points, levels of ambition, technology and disease selection, risk acceptance levels, resources, capabilities and priorities.

Step 3: Create and Execute Innovation Programmes

Regions can prioritize and scale vaccine technology programmes that are appropriate for their current and future health needs, maintaining competitiveness and addressing equity and access issues with targeted basic, clinical and applied vaccine innovation programmes. Regions with limited existing manufacturing capacity can either pursue conventional technologies requiring minimal regional R&D support or leap ahead by utilizing innovative R&D and manufacturing technologies. Regions with more mature and complex environments can support a mixture of applied, basic, clinical and regulatory research and manufacturing capabilities for more diversified, long-term returns. In any case, once established, innovation portfolios can expand, diversify and assemble complementary technologies that create resilience and lower costs through scale, shared facilities and cross-functional capabilities.

To enable innovating organizations to manage risk, it's vital to gain a critical mass of skills and manage a portfolio of innovation programmes. Regions can invest in building and strengthening local scientific and research capacity to conduct vaccine R&D. This includes supporting facility construction and equipment procurement, training programmes, infrastructure development and technology transfer initiatives. Costs can be reduced by pooling resources to staff and fund expensive R&D equipment. Facilities with unique capabilities can be established through public bonds or funds from pharmaceutical companies or donors. Regions can directly fund vaccine research with grants, provide tax breaks for organizations engaged in vaccine research, make long-term resource commitments to prevent funding gaps and provide incentives, including indirect tax incentives, for research into diseases of neglect and the targets of public health initiatives.

Finally, regions should engage in international collaboration and cooperation on vaccine R&D. This involves sharing knowledge, resources and data with other countries to address global health and technology challenges collectively, especially for vaccine-addressable pan-regional infectious diseases. Many international organizations, such as NIH, fund research abroad.

Pillar 5

Technology Transfer and Workforce Development

To be cost competitive, regional vaccine manufacturing facilities using traditional, programmable, and generic scaled production platforms and low-cost raw materials must employ a trained and efficient local workforce. Using ex-pat workforces can make final products more expensive to produce and unprofitable to sell at current vaccine market prices. Regional right-sized business models and pooled market demand must be supported by access to technology and low-cost, skilled local workers to compete.

Without sufficient technology transfer, new regional vaccine production will be reliant on either generic technologies with expired patents or will have to fund and wait for domestic regional manufacturers to develop new proprietary methods. The RVMC Framework seeks to incentivize technology transfer to increase regional innovation, economic development, and equity in vaccine access. Efficient, repeatable tech transfer enables IP holders to access new markets more rapidly and improve returns on innovation and product licensing sales.

Path to Implementation

Step 1: Contextualize and Customize the Tech Transfer Process for the Region's Capabilities

IP holders must develop repeatable, foundational tech transfer programmes that are appropriate to the skills and goals of the regional workforce. Transferring vaccine manufacturing technology platforms efficiently, repeatedly, and effectively to a new, local workforce is a complex process. Only through careful planning and collaboration between IP owners and receiving facilities can these programmes be successful. Tech transfer programmes where the IP holder grants a licence without providing instructions are less likely to succeed. IP licensing contracts should incorporate transfer protections and training and communications provisions to defend the technology and brand reputation of the IP holder, while also providing the recipient with continued access to support.

The modularity and standardization of vaccine manufacturing platforms are core drivers of tech transfer efficiency as they enable simpler, more scalable, and repeatable training. RVMC creates a roadmap for two participants: the IP licensors creating transfer packages and the organization receiving the transfer training.

RVMC recommends that IP holders take the following steps to establish competitive tech transfer programmes:

- **Detail standard operating procedures** for all manufacturing processes. Make them as simple as possible to understand and transfer. These documents should be complete, easy to understand, GMP compliant and regularly updated to reflect best practice and any improvements or changes in the technology.
- **Customize training programmes.** Develop comprehensive training programmes that cover the process and support systems end-to-end. Break the comprehensive training programme into customized training modules that are tailored to the local workforce's skills and knowledge base.
- **Implement learning management infrastructure** that enables multimedia support of tech transfer programmes in classroom, remote, digital, on-the-job, and real-time training and assessment of individual and group learning. This flexibility allows workers to select the preferred learning medium and increase the speed and reduce the cost compared to classroom-only tech transfer options. An LMS also monitors absorption of material by the workforce and course feedback to improve course materials, teaching, and regulatory compliance.
- **Continually evaluate workforce.** Tech transfer and training should continue throughout the relationship with the manufacturer. Track the progress of technology transfer programmes and evaluate their effectiveness. Continuously seek to adjust training based on participant feedback, new developments, regulatory requirements, teaching methods and manufacturing best practice to anticipate and address challenges that may arise.

Tech transfer training teams shape foundational IP transfer packages from the corporate IP owner to the precise needs of the workforce being trained. If the IP owner does not offer such customization and training support, transferring the IP of complex processes can be very challenging for unsophisticated regional facilities. To improve success and efficiency, manufacturers should negotiate with the IP holder to assign an IP holder tech transfer team that can offer support. IP holders transferring their technologies should offer the following facility-level support to protect their brand and rights while training the new workforce:

- **Facility assessments and workforce evaluation.** Facility assessments should evaluate the existing infrastructure, inputs, equipment, systems, and regulatory compliance levels at the receiving facility. Worker evaluation should include base training levels (see below) and capability gaps in vaccine manufacturing operations, regulatory compliance, and safety protocols. Tailor the technology transfer and training programme accordingly.

- **Facility-level training modules** that address the specific skill levels and knowledge of the facility's workforce. Employ long-term expert instructors and mentors who have a deep understanding of vaccine manufacturing processes and experience of training. Deploy train-the-trainer programmes so that experienced personnel from the existing workforce train new employees, lowering costs and increasing the frequency of training.

- **Ongoing technical support** and guidance throughout the technology transfer process. This can include sending experienced technicians and experts from the IP owner's organization to work closely with the local team. Encourage knowledge exchange between the IP owners and the local team, including by supporting visits to the IP owner's facilities or organizing workshops and conferences to share best practice and insights. Promote a culture of continuous improvement within the new workforce.

- **Understanding of and compliance with the local regulatory requirements** of the receiving region. Work with local regulatory authorities to ensure that all aspects of the technology transfer adhere to regulatory requirements and standards. Process and operator training, qualifications and documentation are components of standard GMP compliance.

Step 2: Train the Local Manufacturing Workforce to Receive the Technology

Regions and facilities receiving technologies should consider their workforce's skill and the ease of manufacturing technology transfer within their business model, technology platform and site selection criteria (see pillars one and four). As such, vaccine manufacturing platforms that can be right-sized to regional needs should be prioritized. Modular facility expansion enables tech transfer programmes to be rolled out over time from module to module and team to team, lowering their risk, dependencies, and costs. For long-term sustainability, regions should try to build a workforce dominated by local workers. This will ensure cost competitiveness and human and economic development benefits within the region.

Manufacturers receiving technology transfers should assemble a cross-functional leadership team of experts from across the business, including operations, manufacturing, quality control, R&D, regulatory affairs, and engineering, to take responsibility for overseeing the process. The cross-functional oversight team should endeavour to identify potential risks, develop contingency mitigation plans, and conduct regular risk assessments on an ongoing basis during the transfer process. It's best practice to transfer the totality of the technology infrastructure along with the entire vaccine manufacturing supply chain architecture when introducing a new technology. This ensures consistency of training, implementation and troubleshooting throughout.

Regional workforces must have basic skills in and understanding of biotechnology and vaccines to receive and implement tech transfer packages from IP holders. Manufacturers can partner with education institutions, such as local universities and trade schools, to create tailored training, internship and accreditation programmes that build a pipeline of skilled workers, establish a local presence and support permanent basic skillset training.

For more about the foundational skillsets needed across the organization, see the Unabridged RVMC Framework.

Regionally relevant training programmes and access to blended online and in-person training for trainers are vital for workforce development. Collaboration between regional academic institutes, industry, clinical research organizations and international technical partners is highly beneficial in establishing and implementing the necessary workforce development. Several examples illustrate the progress in this regards: DCVMN has catalogued over 300 online courses and this catalogue is open to the public, WHO is working with the Republic of Korea to host a biomanufacturing tech transfer hub, KEMRI is setting up a vaccine manufacturing hub and apprenticeship programme and CSIR (South Africa) is designing a hands-on training course.

Step 3: Embed Regulatory and Quality Skills

Many vaccine tech transfer programmes fail because they don't explicitly incorporate adherence to regional regulatory manufacturing requirements. This is a critical step if the licensing manufacturer wants to gain regulatory approval and meet the procurement and product-label specifications required to sell in the regional market.

For more, see pillars seven and eight, as well as the Unabridged RVMC Framework.

Pillar 6

Supply Chain and Infrastructure

Most of today's vaccine supply chains operate at an individual country or global level. The world's response to COVID revealed problems with that model which led to inequity and restricted availability. From these experiences, the need for a regional ecosystem to improve the speed and robustness of end-to-end vaccine supply chains is clear.

Right-sizing, integrating, and optimizing regional vaccine end-to-end supply chain infrastructure requires a real-time network to be established among the regional vaccine manufacturers, suppliers, health systems, distributors, vaccinators, governments, donors, and health advocacy groups. This network needs to coordinate a great deal, including planning, procurement, manufacturing operations, infrastructure, sales, warehousing, distribution, quality assurance, regulatory compliance, supply control networking, regulation, and policies.

To achieve compliant, coordinated end-to-end supply chains, regions must incorporate supply chain considerations into manufacturing platform selection criteria, product development and regulatory submissions. This will ensure that by the time a product comes to market, the supply chains are ready to support it. Regional supply chain systems should be complementary to global supply chains. Ideally, regionalized supply chains will be a web of mutually dependent nodes that extend across the member states rather than an aggregation of independent nations. Interdependent networks, such as the EU, worked to ensure supply during COVID-19, while independent supply chains were frequently interrupted at country borders during the pandemic.

Path to Implementation

Step 1: Design End-to-End Vaccine Supply Chains Right-Sized to the Regional Market

To create robust, regional, end-to-end vaccine manufacturing supply chains and support infrastructure, regions must:

- **Map states' existing end-to-end supply chains:** Document the current and planned supply, manufacture and warehousing distribution capacities of vaccines for target diseases, both regionally and globally.
- **Simulate the current and envisioned supply chain:** Outbreak and manufacturing response simulations can help identify potential risks and vulnerabilities in routine and pandemic supply chains.
- **Identify critical points of supply chain failure:** Gaps, overlaps, imbalances and bottlenecks in the current supply chain and infrastructure will need to be mitigated by incorporating geospatial data and scenario models with global partners. The objective is to optimize the current and planned supply chain infrastructure and delivery networks, especially in remote and underserved areas.
- **Integrate with regional pandemic preparedness and response plans:** Mitigation strategies will be needed to eliminate identified risks and create contingency plans. This includes assessing possible disruption to the availability of raw materials, transportation issues, pandemic disease outbreaks, geopolitics, workforce illness, financing constraints, vaccine hoarding or hesitancy, and production delays.
- **Develop end-to-end integration plans:** Coordinate plans with manufacturers, health systems and markets at country, regional and global levels to ensure the appropriate balance of supply and demand. Engage with international organizations like the WHO, EU and UNICEF to access technical support and guidance in establishing an effective regional supply chain policy and integrating with global vaccine supply chain players.
- **Implement supply chain risk mitigation programmes:** Regions should develop and implement short-term, regional, risk-mitigation plans to manage risks in current supply chains and improve responses to unpredictable events, such as natural disasters or geopolitical disruptions.

– **Monitor continuously:** Regular risk assessments, simulations and stress tests will identify vulnerabilities in the supply chain network as the region rolls out and adjusts the supply chain strategy.

Putting complex supply chains and support infrastructures in place at the regional level requires continual monitoring and adjustment as implementation proceeds. The process will help regions build their capabilities and capacities, address unmet medical needs and equitable access, provide routine and outbreak vaccine surge capacity, implement support infrastructures and resolve supply and transport challenges.

Step 2: Diversify Vaccine Manufacturing Operations

Regions will need to employ a wide range of manufacturing options if they're to create a sustainable manufacturing ecosystem that's not tied to one specific product, technology platform or operation. To reduce risk, it's sensible to utilize multiple manufacturing platforms supplied by diversified networks at every stage – from raw materials to patient administration.

For more, see the Unabridged RVMC Framework.

Step 3: Establish Inbound Supply Chains and Logistics

Inbound supply chains and logistics feed the region's vaccine manufacturing facilities. They include the raw material suppliers, transport, storage, and utility systems necessary to acquire and convert raw materials into finished goods. Regions will need an end-to-end strategy for inbound logistics that is designed and implemented in tandem with outbound logistics. The below activities help establish robust, agile and efficient inbound logistics:

– **Develop a strategic sourcing strategy:** During licensing or development, vaccine manufacturers should build relationships and qualify suppliers to lower costs, accelerate innovation, comply with regulations and pharmacopoeial and quality standards, reduce working capital requirements and secure supply.

– **Diversify the supplier base:** A diverse supplier base for critical components and materials can reduce reliance on a single supply source, improve negotiating power and minimize the impact of supply chain disruptions. Long-term contracts and bulk purchasing options can also help ensure a stable supply of raw materials.

– **Create supply-chain redundancy and resilience:** Map critical pinch points and diversify supplier sites, create supply chain redundancies, and strengthen infrastructure to improve resilience and reduce vulnerabilities during emergencies. This ensures an adequate buffer of critical materials to mitigate supply disruptions.

– **Manage supplier quality:** Manufacturers should invest in quality control processes and track ingredients and batch lots to build supplier quality ratings and ensure suppliers meet regulatory reporting and audit requirements throughout the network.

– **Collaborate with infrastructure providers:** New or updated infrastructure requirements for key regional raw materials must be coordinated with the relevant suppliers, including warehouse, transport, waste management and laboratory providers to ensure all parties can handle the amended requirements.

Step 4: Establish Outbound Supply Chain Distribution Networks

Outbound supply chains include the storage and shipment of final vaccine products through regional and extra-regional logistic networks that supply the market during pandemics and normal times. To prevent outbound supply chains from being disrupted by country export controls, regions should create efficient, regional, cross-border supply chains, as well as transport, warehouse, and vaccine administration infrastructure. Requirements such as roads and warehouses should be included in regional funding plans and considered in tandem with manufacturing capacity expansion. Allocation and distribution should be equitable, as determined by the regional health system and pandemic response plans.

Accurate projected demand forecasts act as the basis for establishing outbound product markets, sizing distribution networks, and allocating vaccines to vaccination sites. As covered in pillar two, to avoid overproduction and wastage or stock shortages, regions must transparently forecast, update, and share with their end-to-end supply chain participants the aggregated market demand for routine and surge vaccines ten years in advance.

1. **Forecast and plan sales and operations:**

- **Work to a single plan.** This will enable regions to coordinate supply and demand along the length of the end-to-end supply chain. When each node of the regional network shares data, works to the same sales and operations plan, responds to the same supply and demand signals and knows how much material is in the system, the downstream supply chain can plan and operate at maximum efficiency, improving equitable access to vaccines.

- **Monitor plan accuracy.** Communicate plans across the supply, manufacturing, and distribution hubs. Accurate predictions can help optimize production schedules, allocate resources efficiently and prevent over- or under-production, all of which also improve equity.

- **Plan surge capacity.** Develop plans for scaling up production, stockpiling and distribution during emergencies or other times of increased demand, such as a pandemic.

2. **Manage transport logistics, warehousing and inventory:**

- **Eliminate regional supply chain infrastructure pinch points.** It's necessary to right-size and integrate the regional outbound supply chain to ensure equity and minimize disruption risks. Optimize distribution hubs and nodes into networks and invest in warehouse, transport, digital and electrical infrastructures for better coverage and faster delivery to key regional areas. Strengthen weak links in the end-to-end supply chain to improve equity and access.

- **Diversify warehousing and transportation options.** Having a range of warehouse capabilities, logistic modes and transport routes throughout the regional supply chain – from finished goods production to vaccination centres – will help avoid single points of supply and delivery failure.

- **Optimize geographic distribution network coverage.** Regional demand and health allocation needs during routine and pandemic times should be key factors in determining the capacity and geographic placement of regional manufacturing and distribution hubs.

- **Invest in support infrastructure and technology.** Governments and donors can assist regional manufacturers and suppliers by investing in support infrastructures, such as roads and electricity, and technologies, such as telecoms and IT, to open up and streamline production and distribution operations.

- **Track vaccine lots from factory to arm.** Real-time tracking and IoT technologies can monitor inventory levels and ensure timely replenishment.

- **Optimize warehousing.** Dynamic warehousing strategies can reduce storage costs, reduce wastage and improve inventory turnover.

- **Optimize stock levels and economic order quantities.** Safety stock and buffer strategies can handle unexpected demand surges. Economic order quantity calculations can help maximize vaccine manufacturing batch run efficiencies.

- **Upgrade environmental monitoring and cold chain infrastructure.** Environmental monitoring technologies are needed to track cold chain excursions. Additionally, regions should invest in cold chain infrastructure, including refrigerated trucks, storage, and vaccination facilities.

Step 5: Implement End-to-End Supply Chain Information Systems, Data Integration and Digital Automation

Regions can orchestrate end-to-end regional vaccine supply chains by collecting information at nodes throughout each supply chain. This information can help formalize a single source of truth that can inform strategies for optimizing manufacturing and supply chain operations, supply and demand forecasting accuracy and risk-mitigation activities. Regions should avoid relying on a single source of supply.

For more, see the Unabridged RVMC Framework.

By implementing these steps, tools and techniques, regional vaccine manufacturers, suppliers, health system vaccinators, governments, donors, and other stakeholders can work together to establish an efficient, resilient and responsive end-to-end vaccine supply chain network that can effectively respond to the pandemic and routine vaccination needs of their member states, increasing equitable access and improving public health outcomes.

Pillar 7

Product Regulation

A critical enabler for bringing a product to market is the regulatory approval processes that manufacturers have to navigate on a country-by-country basis. Harmonizing approvals across multiple countries to allow for a single submission, joint review and shared recommendations can reduce both the time and cost to manufacturers, thereby incentivizing them to invest in that region's manufacturing and supply base. Countries within the region will need to collaborate to build trust in and reliance on a common regulatory authority. By focusing initially on harmonizing the primary and secondary laws governing vaccines – as opposed to an unfocused scope that attempts to achieve agreement across all medical countermeasures –, regions will increase the likelihood of consensus and success. For example, the African Medicines Agency is currently being established as a specialized agency of the African Union dedicated to improving access to quality, safe and effective medical products in Africa. Leveraging the existing regulatory frameworks of successful regions (see EU discussion below) can help accelerate these efforts. Additional mechanisms can also be considered, including mutual and unilateral recognition, emergency use authorizations and joint assessments.

Path to Implementation

Harmonize Safety and Quality Regulations Across Member States

Regional authorities will need to work with international and national bodies to develop and harmonize regulatory pathways and procedures that reflect the risk benefit and responsiveness to disease burden in the region. The following best practice will help accelerate access to vaccines without compromising safety or quality:

- **Joint review process:** To minimize approval times and costs, the region must develop a unified, harmonized approach with a single dossier submission, review and approval process. This regional assessment process expedites approvals, reduces the time to market for regionally manufactured products and ensures quicker access for all countries in the regional framework.

- **Reliance and mutual recognition:** Member state regulatory authorities should apply WHO maturity-level standards to select the states within and beyond the region whose market authorizations, trade policies and manufacturing compliance standards they will accept and recognize. Mutual recognition of another state's approved product labels can expedite the availability of vaccines, create accepted standards of vaccine ingredients and final product testing, and lower costs and barriers to enter markets. Regions could use the most mature national regulatory authorities in the region to support other, less mature authorities through joint reviews and assessments of the products, accelerating their entry to market.

- **Fast-track approval processes:** Regulatory agencies in regions and member states should fast-track approval processes through joint assessments, emergency use authorizations and expedited reviews to ensure the timely availability of vaccines while maintaining safety standards. Each region is unique in terms of its needs and legal frameworks, thus regional perspectives are required to successfully harmonize the regulatory environment.

- **Regional regulatory flexibility:** Regions must develop benefit-risk criteria for vaccines both in development and marketed that reflect the health needs and vaccine production capabilities of the region. In times of exceptional need within the region but not the world, member states and regions may choose to license, develop, approve, purchase, and regulate vaccine solutions that are tailored to the region.

    - **Emergency response protocols:** By developing and regularly updating emergency response protocols, a regional network can quickly adapt to unforeseen events, such as sudden disruptions in the supply chain.

    - **Emergency use authorizations (EUAs):** Regional and member state regulatory authorities must establish frameworks for streamlined approvals during emergencies. This can speed up the authorization process for new vaccines – or modifications to existing ones – in response to regional population health needs and disease vectors. Regions can consider expanding rolling submission and decentralized trial regulatory and operating capabilities to support accelerated reviews during EUA.

- **Quality control and compliance:** Ensure rigorous quality control measures and compliance with international regulatory standards. Maintaining high-quality standards throughout the supply chain is essential for ensuring the safety and efficacy of vaccines.

Regions will need to focus on primary laws (treaties) and secondary laws (regulations, directives, decisions, recommendations, and opinions) that ensure consistently safe, high quality and effective vaccines are produced locally. The legislation list below is a starting point for regions building a framework based on EU regulations:

1. **Regulation of vaccine products** comprises rules for the authorization, marketing, and distribution of vaccine products for human use in the region. Member state regulatory authorities should apply WHO maturity-level standards to select the states within and beyond the region whose market authorizations, trade policies and manufacturing compliance standards they can recognize and rely upon. Though it's desirable for each regulator to reach maturity level 3 for vaccines, it's possible to regulate at the highest standards even if few regional member-state national regulators reach this maturity level. Working together with principles of regulatory reliance and recognition, regional decision-making expedites the availability of vaccines, creates accepted standards of vaccine product specifications, claims and labels, defines final product testing and lowers the costs, barriers, and time to enter markets. Member states interested in improving maturity levels should refer to the WHO's global benchmarking tool. Some of the established global standards in vaccine regulation include:

    - **WHO prequalification (PQ)** – Evaluates the quality, safety and efficacy of vaccines approved by mature national regulatory authorities to the WHO programmatic suitability criteria for use in LMIC settings. International organizations like UNICEF and Gavi require vaccine manufacturers to qualify suppliers. This global standard helps maintain confidence in the quality of vaccine products but can add years and costs to introducing a vaccine and pose a significant barrier that prevents new regional vaccine manufacturers from quickly entering global markets. While there are attempts being made to expedite WHO PQ approvals, regions can set their own standards for accelerating entry to regional markets without compromising safety, quality, or efficacy. This will maintain public trust in vaccines, ensure an early return on investments and balance the risks and benefits of proposed vaccines in the region.
    - **Vaccine-specific guidelines** – Regions can create specific regulations based on the vaccine manufacturing process. The FDA, EMA and WHO all have specific regulations for manufacturers of live attenuated and whole virus production. RVMC recommends that regional regulatory authorities adjust to the new risks and benefits of established and emerging vaccine manufacturing technologies to de-risk their regulatory uncertainties and facilitate their introduction.

2. **Pharmacovigilance regulations** to govern the collection, assessment and monitoring of adverse drug reactions and safety data for vaccine products. This includes reporting adverse drug reactions, signal detection, risk management plans, periodic safety update reports and product recalls, warnings, or exclusions. Pharmacovigilance aims to ensure that the benefits of vaccines outweigh their risks and protects public health.

3. **Good manufacturing and distribution practices (GMP and GDP)** – Regions and common markets must ensure that vaccine manufacturers adhere to strict quality standards in the production and distribution of medicinal products. Regions must have their own regional standards or adopt global WHO standards and systems to ensure the quality of product manufacturing and distribution by strengthening GMP regulations.

4. **Human clinical trial regulations** to simplify, streamline and mutually recognize the approval process for new vaccine products. These regulations harmonize the rules for conducting clinical trials across member states in a region. In an ideal regional vaccine ecosystem, such regulations will control multi-country, coordinated clinical trials, ensuring the safety, quality, and efficacy of locally produced vaccines.

5. **Data-sharing regulations** – Regions must establish mechanisms for securing and sharing product, clinical, public, and individual health data and surveillance information to monitor vaccine safety and efficacy. Regions can also consider developing agreements related to sharing public health data among member states, including epidemiological surveillance, disease reporting, pandemic preparedness, medical countermeasures, emergency response plans, immunization programmes and vaccination rates to improve benefit-risk assessments in market approval decisions.

6. **Pediatric vaccines** – Special regulations may be required to address the development and authorization of childhood vaccines to improve the availability of safe and effective pediatric treatments.[18]

The European Union regulations passed since the establishment of the European Medicines Agency create a comprehensive framework with guidelines that can serve as a basis for other regions. The framework ensures that the safety, efficacy, and quality of pharmaceutical products is maintained throughout a vaccine's product life cycle.

The last three points listed above are only required for regions interested in regulating the clinical development and approval of novel drugs. Some regions may choose to postpone these regulations to more rapidly establish a minimum viable regulatory framework that focuses on regulating approved and available vaccines.

Gaining complete member state alignment across all regulatory areas may not be feasible initially. Instead, regions can select the critical areas of common interest and agreement among countries for vaccine authorization. For example, EUA regulation for collectively reviewing and approving vaccines during outbreaks and pandemics might be a good starting point for a newly formed region. This can be achieved by adopting global standards and guidelines but articulating a regional decision-making process (instead of country-by-country decisions) for quicker approvals and access to vaccines in emergency situations. These regulations can then be extended to other vaccine approvals once trust and confidence in regional decision-making grows with the experience of working together. Ensure that the regulations are designed to be extendible (see pillar eight, Governance, below) so they can grow with regional needs over time and incorporate and customize the regulations required for sustained success.

To achieve a minimum viable regional vaccine regulatory framework, the RVMC Framework encourages harmonized regulations in the following areas:

- **GMP and GDP quality standards** – Ensure consistent vaccine product quality in the regional market.
- **Marketing authorization** – Put in place effective procedures for regional marketing authorization. Centralized or reliance market authorization procedures require a regionally empowered vaccines agency or a mutual recognition framework for approval to ensure a single submission, review, and approval process for the entire region. These procedures allow scaled operations to produce to standard labels and claims across regional common markets.
- **Pharmacovigilance** – Report adverse events associated with vaccines to ensure safety is maintained after approval.
- **Batch release** – Manufactured vaccines must undergo batch release by a qualified regional authority and lot testing at a qualified regional laboratory before entering the market. For example, a model for sharing resources and reliance for vaccines and biologicals across competent WHO-recognized labs has now been proposed for Africa.
- **Regional access** – The region must work towards a collaborative process which gives access to markets once products are approved by regional authorities. Ideally, regional access ensures that member states have identical product specifications and labels for authorized vaccines. This scenario overcomes the barriers posed by current country-by-country product registration processes.

The region must work during non-pandemic times to ensure regulatory standards are harmonized, a good regulatory governance structure is in place and that the workforce is trained and qualified. This preparatory work will mean the region is prepared to handle outbreaks and pandemics while also supporting the regional vaccine ecosystem.

When creating a viable regulatory framework, some regulations may initially remain with individual member states, including:

- **Pricing and reimbursement** – Each country may negotiate prices and reimbursement policies separately, leading to differences in access and affordability.
- **Vaccine distribution and administration** – Operations can differ between member states, affecting the availability and accessibility of vaccines.
- **Vaccination schedules and policies** – These may vary based on members' healthcare priorities and epidemiological situations.
- **Data protection and privacy regulations** – Variance here may impact how vaccine products and patient data are managed.

Regions must work continuously to harmonize technical regulations across member states if they're to ensure a unified approach to vaccine safety and quality. However, some variability in non-scientific matters, such as pricing, reimbursement, and healthcare policies, are likely to remain due to the natural diversity of healthcare systems and priorities within a region.

See the Unabridged RVMC Framework for regional regulatory considerations in trade and IP.

Pillar 8

Policy and Governance

This pillar addresses two critical components of a regional vaccinee manufacturing ecosystem: establishing a vaccine manufacturing region and developing policies and governance processes. The former entails creating a secretariat at a host institute within the region with a mandate for vaccine manufacturing governance. The latter involves setting up a common, regional, vaccine manufacturing collaborative and market.

Path to Implementation

Step 1: Set Governance Strategy and Establish Regional Initiatives

Regions may elect to establish or leverage a regional governing body that oversees multilateral agreements, technology licensing agreements, common market regulations and the mutual recognition and harmonization of product approvals. The governance strategy for such a body can build on existing regional or cross-border agreements and governance structures, thereby accelerating the formation and implementation of regional initiatives. Such an initiative could be hosted at a permanent institution in the region and run by a secretariat structure as, for example, PAVM hosted at Africa CDC.

Alternatively, where no such permanent regional institution exists, a secretariat could be hosted at a country institute or through a rotating arrangement between countries. Treaties between two or more nations can also be used as a foundation to broaden governance and add additional member states that have compatible health system and vaccine supply needs.

Countries will need to empower assigned leaders with clear roles and responsibilities to create and manage regions. Regions must decide which areas of governance can be resolved by collectively recognizing member state decisions and which areas may need a legal process framework or a new regional agency. Finding the right balance will require skillful diplomacy and knowledge of laws and policies to gain consensus among the region's leaders. To make this achievable, it's critical to limit the scope of governance to regional vaccine manufacturing only.

Once a governance strategy is in place, regional institutions must be empowered to communicate, manage and resolve open issues efficiently, rapidly and fairly. A well-defined secretariat structure and a process for expanding the production of regional vaccines will enable regions to develop a vision and implementation roadmap. Regional governance institutions must delineate processes that address subjects such as who can raise issues and which governance processes and institutions are responsible, as well as providing a resolution pathway that all parties can agree to and implement. This will allow for more rapid, equitable and consistent responses to issues as they arise within regions.

Step 2: Implement Regional Policy Framework

Regional vaccine manufacturing and markets can be governed through a combination of regulatory frameworks, international cooperation, public-private partnerships, and ethical policies that ensure equitable access and distribution. While some governance processes can be managed more effectively at a national or global level, there are many opportunities to improve vaccine operations and health through regionalization. In addition to stringent regulatory authorities for vaccine product oversight, regional organizations can introduce new vaccine manufacturing governance models with the potential to streamline existing country-based governance.

See the Unabridged RVMC Framework for IP protection recommendations.

To implement common market regulations across member states, regions can use regional authority agreements, rulings and precedence. Regional market regulations are designed to create seamless economic spaces that eliminate trade barriers and safeguard fair competition, allowing small country markets to pool demand and support new vaccine manufacturing capacities. New regional governance will be required to achieve a single regional vaccine market among member states' health systems, vaccine manufacturers, donor organizations, NGOs, regulators, and procurement organizations.

Governance and regional policy frameworks can create regional markets that eliminate tariffs and non-tariff barriers that restrict efficient, transparent, and equitable healthy markets for vaccine products and their supply chain.

See the Unabridged RVMC Framework for free trade recommendations and non-trade barriers that can be eliminated by regional action.

Regions must establish primary and secondary laws that serve the minimum viable regulatory framework necessary to promote the free movement of vaccine goods, services, capital, and people among member states. Well-regulated, high-quality, safe, and efficacious vaccines require a common, aggregated healthy market to achieve scaled and competitive production levels. The specific regulations needed to create and shape a common market vary depending on the level of product unification and mutual procurement that's desired across the market. Regional secretariats need to identify and finalize a list of those desired regulations to prepare a roadmap that addresses all the barriers to a common regional market.

To implement an effective governance structure, regions can use pillar-based initiatives that help ensure their framework is managed in a consistent way through regional governance processes, working towards their policy objectives as the initiative matures.

Conclusion and Outlook

Recap

The key issues, challenges and opportunities presented throughout this framework document all relate to the governance of access to vaccine manufacturing technology, markets and financing. Regional initiatives to improve access are critical in catalyzing innovative solutions in the short term and economically viable, equitable and enduring solutions in the long term. Together, the RVMC pillars drive and support technology diversification, workforce development and supply chain management. Regions can successfully build a portfolio of manufacturing technologies to diversify risk, with prioritized investments in modular manufacturing driving robust, proven platforms.

Innovative, right-sized and flexible regional vaccine manufacturing operations, supply chains and support infrastructure will increase sustainability and reduce the risks and inequities incurred by the current, brittle, hub-and-spoke models that suffer from many single points of failure and are vulnerable to breakdowns during outbreaks. These technologies, combined with seamless end-to-end information sharing of capacity utilization, product quality and product availability along the vaccine supply chain, will enable regional manufacturing to remain resilient, flexible, and agile.

Supply: Access to Technology

Regional reach and scale can improve access to the advanced technology, manufacturing facilities, supply chain, infrastructure, and workforce skills required to produce vaccines.

Advanced technology – Regional models provide better support for a full suite of technologies that can fight infectious disease across a region. Current vaccine manufacturing is highly concentrated, with decisions on vaccine allocation coordinated through a small number of key global and national players that control the IP of branded vaccines as well as the manufacturing know-how and scaling capabilities for biosimilar vaccines. Current, centralized, global hub-and-spoke models focus on a single vaccine technology platform and create the potential for vaccine nationalism and vaccine diplomacy[19] that results in inefficient and inequitable distribution. Regions can address IP issues in a fair and diplomatic fashion that preserves the benefits due to IP developers while ensuring access to the technology in places of greatest need.

Regions offer scale and resources that can accelerate the development and acceptance of innovative programmable vaccines. New programmable vaccine technologies can quickly change the landscape by enabling vaccines to be developed rapidly with comparatively low capital investment. They can also deliver a faster response to new diseases, lower dosages, and a greater ease of producing multivalent vaccines and other bio-engineered products which further expand regional vaccine manufacturing technology portfolios, address diseases of neglect and prevent regional disease outbreaks. Regions can make enhanced and more consistent contributions to antigen libraries and accelerate the timeframe from innovation to market. In addition, they can scale up the production of traditional vaccine technologies which can be the best choice for specific diseases.

Manufacturing capacity – This framework supports the expansion of facilities on greenfield and brownfield sites for vaccine manufacturing technologies. The scale and capital investment required can be high and timelines long. Most countries cannot support the minimum economic scale required for cost-effective production. Therefore, joining with other countries to form regions makes scaled vaccine manufacturing facilities viable.

The framework is designed to support the equitable delivery of vaccines under both routine and pandemic conditions. Responding to outbreaks of disease requires on-demand, flexible capacity expansion to meet surge requirements and avoid price spikes and inequitable access. This can be better managed at a regional level, and using this framework offers regions options to finance, manage and access surge capacity as needed.

Supply chain – Vaccine manufacturers require inbound access to quality raw materials and outbound support through environmentally controlled and efficient end-to-end delivery networks. A robust, networked supply chain – where vaccines are produced closer to places of need across a region – doesn't suffer from the single point of failure risks of global and national hub-and-spoke systems. By depending on each other to supply their vaccine products, member states can benefit from a resilient and networked supply chain.

Tech transfer and workforce development – Regions can enable a more repeatable, scaled, and cost-effective tech transfer environment for IP holders. Employing a local vaccine manufacturing workforce with regulatory compliance skills helps a region become cost competitive and self-reliant. Compared to global hub-and-spoke solutions, regions can offer a more consistent regulatory environment and improved, focused training options during tech transfer to speed up workforce scaling and skills transfer. New regional facilities and line extensions will need to invest in multi-modal learning management systems to establish a culture of continuous learning and improvement.

Demand: Access to Markets

Regions are critical to the aggregation of demand and the efficient, transparent procurement of vaccines using Gavi's Healthy Markets Framework. Once achieved, these objectives enable fact-based, equitable responses to routine and pandemic demand.

Demand aggregation – A regional approach enables individual countries to join together, creating a combined market with sufficient demand to satisfy the minimum scale requirements of a single vaccine manufacturing facility. Regions are best placed to sync demand aggregation with sufficiently scaled suppliers to maintain consistent pricing and equitable distribution during pandemic and routine times. The infectious disease outbreaks that drive surge demand do not stop at country borders. Regional markets can respond more effectively, equitably, and faster than individual countries or distant global suppliers.

Efficient and equitable procurement – A lack of regulatory and product consistency across national markets can make them fragmented and uneconomic. This framework enables regions to generate sufficient market demand to absorb production from right-sized manufacturing facilities producing approved, identical products and labels across national borders, therefore achieving sustainable, low-cost, and appropriately scaled vaccine manufacturing operations. Regional pooled purchasing creates efficiencies of scale and negotiating power for volume discounts and broader access to more vaccines.

Healthy Markets Framework – In a completely free market, the ability to pay, rather than health need, drives allocation, meaning wealthier countries can afford to pay for preferential access to vaccines. By establishing market-shaping mechanisms, regions can direct the flow of capital to meet the specific health needs of their populations. As such, regionally aggregated demand creates scale efficiencies, reliability, simplified transactions, and equitable distribution at any time. Regional markets can also respond more effectively and rapidly to infectious diseases that spread beyond country borders.

The RVMC Framework fosters collaboration between regional producers and buyers to maintain demand and innovation at sustainable prices, thus increasing vaccine equity and ensuring consistent and predictable pricing. That predictability and sustainability allows planned facility expansions to be financed through advanced purchase commitments during routine times and capacity reservation agreements during pandemic outbreaks. Predictable, sustained regional baseline demand also improves the planning and economics of ongoing vaccine plant operations.

Capital: Access to Financing

Regions can improve access to sustainable capex and opex and market-uptake financing by forming public-private partnerships that can achieve triple bottom line benefits at lower costs and risks than global or national programmes.

Access to capital – The timing and risks of capacity expansion and market-uptake financing differ and require access to various sources of capital. A significant capacity expansion requires both financing of the facility and the pre-purchase of produced vaccine. Typically, facilities should plan a roughly 50/50 split over the investment timeframe, especially for greenfield facility expansions. For example, if a greenfield site costs $500 million to build, another $500 million is likely to be required to finance market uptake until the facility becomes self-sustaining.

Financial and social benefits – The benefit-cost ratio of proposed projects increases up to six times for regions compared with producing for national markets. Nationally proposed vaccine manufacturing projects that appear only marginally economical or even unprofitable in a feasibility study can become profitable when they're set in a regional ecosystem. The returns on these investments will meet the mandates of multiple public, private, and donor funding sources. Private financiers recognize economic profits and returns directly, while public financiers must be positioned to recognize the returns arising from the vital role vaccines play in protecting public health and improving economic productivity. Regional financing mechanisms are important providers of initial capital for manufacturing facilities, de-risking industry investment and partially sustaining the facilities and demand. Unrestricted donations from NGOs can give additional flexibility in targeted investment areas while supporting the donor's mission and increasing access to contributors across the region.

Reduced risk – Regions applying the RVMC Framework can de-risk vaccine manufacturing capacity investment in two ways: by offering a comprehensive roadmap that creates sustainable business models which are supported by public and private financing, and by mitigating operating, governance, regulatory, technical and market risks and the conditions that contribute to vaccine inequity and socio-economic unrest.

Looking Ahead

The pillars of this framework need to be established in concert with each other and adapted to regional needs and ambitions. As regions execute against their roadmaps and advance along their respective maturity journeys, they can also apply the lessons learned for vaccine manufacturing to other industries. Adjacent industries supporting regional medical countermeasure programmes, such as therapeutics, diagnostics and personal protective equipment, and orthogonal bioprocessing and health industries can all benefit from similar public-private collaboration. As a result, what began as an effort to provide regional self-sufficiency for pandemic response scenarios can morph into a paradigm for improving health outcomes, accelerating the availability and acceptance of new technology platforms and, ultimately, sustainable economic development. Consequently, this framework serves as a template for convening public and private sector leaders to address nothing short of humanity's greatest challenges.

Think globally, organize regionally, and act nationally.

Ambassador Dr. John Nkengasong

Acronyms

Africa CDC – Africa Centers for Disease Control and Prevention

ASEAN – Association of Southeast Asian Nations

CDMO – Contract development and manufacturing organizations

CEPI – Coalition for Epidemic Preparedness Innovations

Gavi – Gavi, the Vaccine Alliance

GMP – Good manufacturing practices

IP – Intellectual property

IFC – International Finance Corporation

LMIC – Low- and middle-income countries

mRNA – Messenger ribonucleic acid

PAVM – Partnerships for African Vaccine Manufacturing

PPP – Public-private partnership

R&D – Research and development

RVMC – Regionalized Vaccine Manufacturing Collaborative

WHO – World Health Organization

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