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Review

Manufacturing platforms for vaccines and biologic drugs in resource-limited settings: Challenges, innovations, and pathways to sustainable access

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ABSTRACT

Introduction: Demand for vaccines and biologics continues to rise across human and veterinary health, yet low-resource settings such as Africa carry a disproportionate burden of human immunodeficiency virus, hepatitis B, malaria, tuberculosis, and neglected tropical diseases. This review evaluates manufacturing technologies and strategies that can strengthen local production capacity to improve biologic access, pandemic preparedness, and outbreak response.

Methodology: A structured narrative review was conducted, guided by the SANRA framework, using peer-reviewed literature published between 2015 and 2026 and retrieved from PubMed/Medline, Scopus, Web of Science, and Google Scholar, supplemented by relevant grey literature on biologics manufacturing in low-resource settings.

Results: No single platform is universally optimal; selection should be matched to local capacity, target disease, and sustainability. Egg-based and cell-culture systems are accessible but limited in speed and scalability, while mRNA platforms adapt fastest yet depend on cold-chain and reagent infrastructure rarely available locally. Recombinant protein and virus-like particle platforms emerged as the most pragmatic compromise, combining thermostability with feasible bioprocessing. Across platforms, sustainable production depended less on the technology than on cross-cutting enablers: modular and single-use manufacturing, digital process control, regulatory harmonisation and World Health Organization prequalification, workforce development, and blended financing. Africa's approximately 1% share of global vaccine supply underscores that equitable access requires these enablers to advance in coordination.

Conclusions: Meeting the growing need for biologics requires capacity building, infrastructure investment, public-private partnerships, and dedicated funding reducing import dependence and improving pandemic readiness, as the coronavirus disease 2019 pandemic made clear.

KEYWORDS

vaccines, drugs, biomanufacturing, Africa

INTRODUCTION

Global demand for vaccines and biologic drugs continues to expand across both veterinary and human health sectors. Africa, having the most developing countries, continues to suffer a disproportionate burden of neglected tropical diseases (NTDs) and other infectious diseases such as human immunodeficiency virus (HIV), hepatitis, malaria, and tuberculosis (TB). Malaria caused an estimated 263 million cases and 597,000 deaths worldwide in 2023, with the World Health

Organization (WHO) African Region bearing about 94% of cases and 95% of deaths [1]. Moreso, HIV and hepatitis B co-infection constitutes 73.8% of global hepatitis B virus (HBV) cases in people living with HIV originating from sub-Saharan Africa [2]. TB keeps on straining health systems with an estimated 10.8 million new cases and 1.25 million deaths globally in 2023 and rising absolute case numbers in Africa [3,4]. NTDs account for 90% of the global burden in sub-Saharan Africa, which, on the other hand, exceeds the burden of malaria and TB [5,6]. With these terrifying and enormous figures with inadequate management, vaccines are therefore essential tools to reduce morbidity and mortality and strengthen health systems across the continent. Asia, Africa, and South America, with their highly projected growth in antimicrobial consumption and demand for animal-sourced foods, are expected to have the highest demand for animal vaccines [7]. In 2023, the global vaccine market reached approximately seven billion doses with a financial value of US$77 billion, driven largely by coronavirus disease 2019 (COVID-19) vaccines and increasing uptake of shingles, human papilloma virus (HPV), and respiratory syncytial virus (RSV) products [8]. According to Ecker and Seymour [9], the projected global demand for biologics manufacturing capacity is expected to surpass 4,700 kilo litres by 2024, reflecting an annualized growth trajectory of more than 10%. Together, these trends highlight that a sustained investment in both human and veterinary biologics is essential to coincide with the rising global health needs to mitigate future health threats. Equitable access to vaccines and other essential medicines remains one of the most pressing challenges in global health [10]. Disparities in access disproportionately affect settings (resource-limited settings – RLS), where supply chains, systemic limitations in infrastructure, and healthcare delivery restrict the availability of life-saving interventions [11]. The COVID-19 pandemic exposed and exacerbated these inequities, with delayed vaccine roll-outs and treatment access gaps leading to preventable morbidity and mortality [11,12]. Reliance on single-source suppliers for vaccines contributed to challenges in achieving vaccine equity globally [13]. Establishing local manufacturing capacity has become a cornerstone for sustaining routine immunization programs that protect populations against pandemics. Binagwaho et al. [14] proposed that strengthening vaccine production in Africa would enhance the continent's capacity for self-reliance, both in routine immunization programs and during public health emergencies, thereby linking local manufacturing to broader goals of self-sufficiency. For instance, the BRICS (Brazil, Russia, India, China, South Africa) countries have pursued vaccine self-sufficiency to address their dependence on foreign vaccines as the region is heavily affected by infectious diseases, which was a threat to survival and development [15]. Vaccine supply chains in developing countries, such as Pakistan and several African nations, are constrained by limited health infrastructure, security challenges, poor data visibility, inadequate cold chain capacity, and frequent inventory stock-outs

[16]. On the other hand, high-income countries pre-purchased excess vaccine doses, which prevented RLS from accessing the market and forced reliance on facilities like COVAX (COVID-19 Vaccines Global Access Facility), which faced challenges due to manufacturers' agreements and export bans [17,18]. Despite these disease burden statistics, LRS such as Africa, the continent produces about 1% of the global vaccine supply, and around 3% of the global pharmaceuticals, and with approximately 70%–90% of imports of medicines used globally [19]. The purpose of this review is to evaluate vaccine and biologic manufacturing platforms that are most suitable for RLS. The paper aims to recognize the technologies and strategies that can strengthen local production capacity through aggregating evidence from peer-reviewed studies, technical reports, and policy documents. This will drive investment, regulatory alignment, and tech transfer to improve biologic access, pandemic readiness, and routine immunization in RLS.

METHODOLOGY

This review has employed a structured narrative review to evaluate vaccine and biologic manufacturing platforms suitable for RLS. To enhance transparency, methodological rigour, and reproducibility, the design, conduct, and reporting of this review were guided by the Scale for the Assessment of Narrative Review Articles (SANRA) and by established guidance on writing narrative-style literature reviews [20,21]. In accordance with these criteria, we explicitly justified the importance of the topic, stated a clear review aim, described the literature search and source-selection process, and supported key statements with appropriate referencing. Although a narrative design was selected deliberately to allow integrative synthesis across heterogeneous technical, operational, regulatory, and policy literature that a strict systematic-review protocol would exclude applying the SANRA framework provided a structured and auditable basis for the methodology described below. Peer-reviewed journals indexed in PubMed/Medline, Scopus, Web of Science, and Google Scholar were searched, complemented by grey literature, such as reports from WHO, Global Alliance for Vaccines and Immunization (Gavi), Coalition for Epidemic Preparedness Innovations (CEPI), and regional health agencies, was also reviewed to capture operationally relevant sources not indexed in traditional databases. The time-frame for inclusion was deliberately set from 2015 to 2026 to capture a decade that encompasses both established and emerging technologies relevant to biologics production.

The inclusion criteria focused on English-language studies and reports that identified manufacturing technologies, infrastructure requirements, or capacity-building initiatives in RLS. Publications that addressed only clinical efficacy or therapeutic outcomes, without reference to manufacturing processes, were excluded. Additionally, the reference lists of key articles were manually screened to identify supplementary sources. Search terms combined controlled

vocabulary and free-text keywords related to “vaccine manufacturing,” “biologics production,” “infrastructure,” and “capacity building in RLS.” Boolean operators were applied to refine the results, and filters were set for English-language publications within the defined time-frame. Duplicate records were removed, and titles and abstracts were screened independently before full-text assessment.

Extracted data emphasized platform type, scalability, cost considerations, quality assurance mechanisms, and regulatory compliance frameworks. Case studies such as COVID-19 were prioritized to illustrate practical challenges and enabling innovations in low- and middle-income countries (LMICs) contexts. Policy documents were separated from technical literature to ensure contextual relevance and alignment with global health priorities.

The analysis integrated a comparative synthesis of manufacturing models by highlighting enabling factors for sustainable production. Thematic organization was structured around four domains: (i) infrastructure adaptability, (ii) scalability of technologies, (iii) cost and quality assurance, and (iv) regulatory alignment. This approach fostered integration of technical, operational, and governance perspectives and provided a balanced assessment of feasible strategies for strengthening biologic manufacturing capacity in resource-limited environments.

STATE OF KNOWLEDGE

Definition of terms

Vaccine – is a biological product that contains an antigen (e.g., viral, bacterial, fungal, parasitic), which mimics the disease without causing the actual disease, but to train or stimulate an immune response so that when the actual disease strikes, antibodies are released immediately from immune memory, protecting the organism from severe illness or fatality. Vaccines can also contain adjuvants, diluents, preservatives, colorants, and stabilizers.

Biological drugs – these are medicines that are derived from living organisms (e.g., bacteria, yeast, or mammalian cells), rather than conventional drugs which are chemically synthesized. They are typically large, complex molecules such as proteins, monoclonal antibodies, or vaccines.

Manufacturing platforms – these are technologies which utilize living systems or synthetic methods in order to produce therapeutics (vaccines or biological drugs). They include cell-based, genetic (mRNA, DNA), microbial, viral, and protein-based approaches.

Resource-limited settings – there are environments with constrained access to healthcare infrastructure, funding, and skilled personnel. They often have challenges such as inadequate laboratories, supply chains, and cold-chain systems for vaccines and biological drugs.

Vaccine and biologic manufacturing platforms

Vaccine manufacturing technologies and platforms have evolved over the years to overcome limitations, reflect technological advancements, and address ongoing concerns [22]. Vaccines can be classified based on their ability to replicate in the host (e.g., live versus dead vaccines) and/or the technology/platform used in their manufacturing. Live attenuated, or replication-competent attenuated vaccines are prepared from weakened pathogens, where the virulence indicated by severity or harmfulness of the disease is considerably reduced [23]. However, the attenuated pathogens mimic natural infection in their ability to infect, replicate, and release in the host [24]. The ability to maintain the pathogens' replication potential without causing disease or reversion to virulence is a key consideration for this technology. Inactivated vaccines are derived from a killed form of virulent pathogens and typically stimulate an antibody-mediated immune response [25]. The inactivation process is mediated by chemical or physical methods or a combination of both. Examples of chemical mediators used for pathogen inactivation include formaldehyde, glutaraldehyde, ascorbic acid, hydrogen peroxide, β-propiolactone, and ethylenimine derivatives [26]. Physical inactivation is typically accomplished by heat and/or pH denaturation, ultraviolet light and/or gamma irradiation, or other methods [26].

Traditional egg-based and cell culture systems

The most appropriate and simplest viral vaccine mass production technology, in the 1940s, was the use of embryonic eggs as "*mini factories*" for the influenza vaccine and later adapted to the development of other vaccines, such as New Castle and infectious bursal disease virus (IBDV) vaccine [27]. In this technology, the fertilized embryonic eggs are inoculated with the virus and incubated to allow the virus to replicate. The eggs are then broken and the contents harvested, the virus separated, purified, and in some instances inactivated, then formulated, filled into vials or syringes, and packaged [27]. This technology is estimated to produce one vaccine dose per 1 to 2 eggs [22]. Egg-based vaccines still account for over 80% of influenza (flu) vaccines produced globally [27]. Egg-based vaccine technology goes beyond seasonal flu shots and nasal sprays to include vaccines for yellow fever and Q fever. Among these, the flu vaccines are the most commonly used because of the recurring threat of seasonal influenza [28]. This manufacturing technology is well established and still in use, although it has some challenges; Firstly, the egg-based vaccines have some shortfalls in terms of resources needed and the quality of the end product. Secondly, Supply Chain: Egg-based production requires a steady supply of fertilized eggs. For influenza alone, vaccine production capacity is about 1.53 billion doses annually, which consumes millions of eggs. Therefore, disruptions in supply chains could threaten vaccine availability [29]. Third, egg-based vaccines and allergy concerns, egg-based vaccines raise questions among individuals with egg allergies. Fortunately, influenza vaccines usually contain only

trace amounts of egg proteins, insufficient to cause reactions in most cases. Purification steps during manufacturing further reduce residual proteins. Animal cells (examples: HeLa cells, Vero cells, MDCK, Chicken embryo fibroblast) are grown in vitro and infected with the virus. The virus multiplies in the cells and also causes cell lysis. Then, the virus is separated via centrifugation and inactivated via heat or chemical treatments using formaldehyde or β-propiolactone [28]. Both embryonated eggs and cell culture technologies are very important in resource-limited environments and are easily adoptable and scalable [29]. However, these alternatives are more expensive than egg-based vaccines. While they guarantee faster production, the resources required can be out of reach, especially for developing nations that do not have access to even the cheaper egg-based vaccine production infrastructure. While newer technologies produce viral strains very similar to human strains, there is still room for variation, especially with cell culture-based vaccines, which can be affected by mutations in host cells. Moreover, some cell culture-based technologies yield low viral titers [30].

Recombinant protein, viral vector platforms

Recombinant protein vaccines, also called recombinant subunit vaccines, are formulated using defined protein antigens that can be produced in heterologous expression systems. A great number of expression systems can be evaluated depending on the antigen to be produced: bacteria, yeasts, insect cells, mammalian cell lines, or plants. The challenge of the industry today is supporting the scale-up of these various expression systems and developing downstream processes tailored to disease-specific antigens [31]. Arguably, the most appropriate technology for RLS would be recombinant protein vaccines, since the final product is thermostable enough to be distributed through standard -20 to -80°C cold chains [30]. The main disadvantage is that they are relatively slow in development. Viral Vector vaccine has the advantages of having high immunogenicity with long-term effects, including excellent cell-mediated immunity, and relative thermostability. It is good for RLS, but is more complex to produce [31]. Recombinant technology involves manipulating genetic material. It takes a specific gene from one organism and inserts it into another, allowing the recipient organism, or host cell, to produce the protein encoded by that gene. In vaccines, this protein is typically an antigen from a disease-causing microbe. These host cells then act as biological factories, mass-producing the desired protein. This process bypasses the need to grow the actual pathogen, offering a precise method for vaccine component creation [31].

mRNA platform

mRNA vaccines have the quickest development time from sequence to candidate (days to weeks), but the infrastructure for this technology is nearly impossible in RLS [32]. The complexity of mRNA vaccine production involves in vitro transcription enzymes, nucleotides, and lipid nanoparticles

(LNP) formulation, which rely on specialized reagents and equipment with supply chains [33]. Another challenge is the issue with cold chain due to its negative charge; mRNA does not easily enter the cells. It can be rapidly degraded by nucleases such as the enzyme RNase. LNP encapsulation, which is used in the current mRNA-based COVID vaccines, helps mitigate this problem, as do other methods involving the substitution of modified bases or the design of the mRNA. Alternatively, physical methods such as electroporation can be employed. This approach has gained traction in ex vivo-administered therapeutic cancer vaccines but is not highly efficient. Distribution of the vaccine is another issue, as current mRNA vaccines require frozen storage. Alternative methods, such as lyophilization, are under study [30]. Manufacturing also presents issues; one of the main challenges in mRNA processing is the lack of dedicated equipment and consumables fit for the relatively small volumes and large size of mRNA molecules, compared to traditional recombinant proteins. There is also room for improvement in technology development to enhance scalability and process consistency [34].

Virus-like particles platform

The term virus-like particles (VLPs) refers to particles that self-assemble as a result of the expression of proteins encoding capsids, cores, or envelopes of viruses or even preparations of mono-layered particles derived from a multilayered virus [35]. These VLPs mimic the structure of the virus, effectively training the immune system. Specific influenza vaccines and some protein-based COVID-19 vaccines also utilize this platform. Symmetrical particles formed from non-viral or artificial proteins can also be considered VLPs; in this case, symmetry refers to the way the capsomere units are geometrically organized. However, this category of VLPs is not discussed in this review. Additionally, VLPs self-assemble into particles that resemble or mimic the structure, size, and symmetry of original viruses; however, VLPs cannot replicate as they lack a genome and replicases [35]. Detailed descriptions of VLP structure, immunogenicity, and expression as they relate to vaccination are reviewed elsewhere [35].

Platform technologies enabling rapid adaptation to new pathogens

Platform technologies for rapid pathogen adaptation are based on standardized, modular, and well-characterized ‘backbone systems’ that can be rapidly adapted to new threats, like in Figure 1, often shortening vaccine development timescales to less than 100 days [36]. These systems enable manufacturers to change only the genetic or protein sequence of the new pathogen while retaining the same production process, quality, and formulation [36].

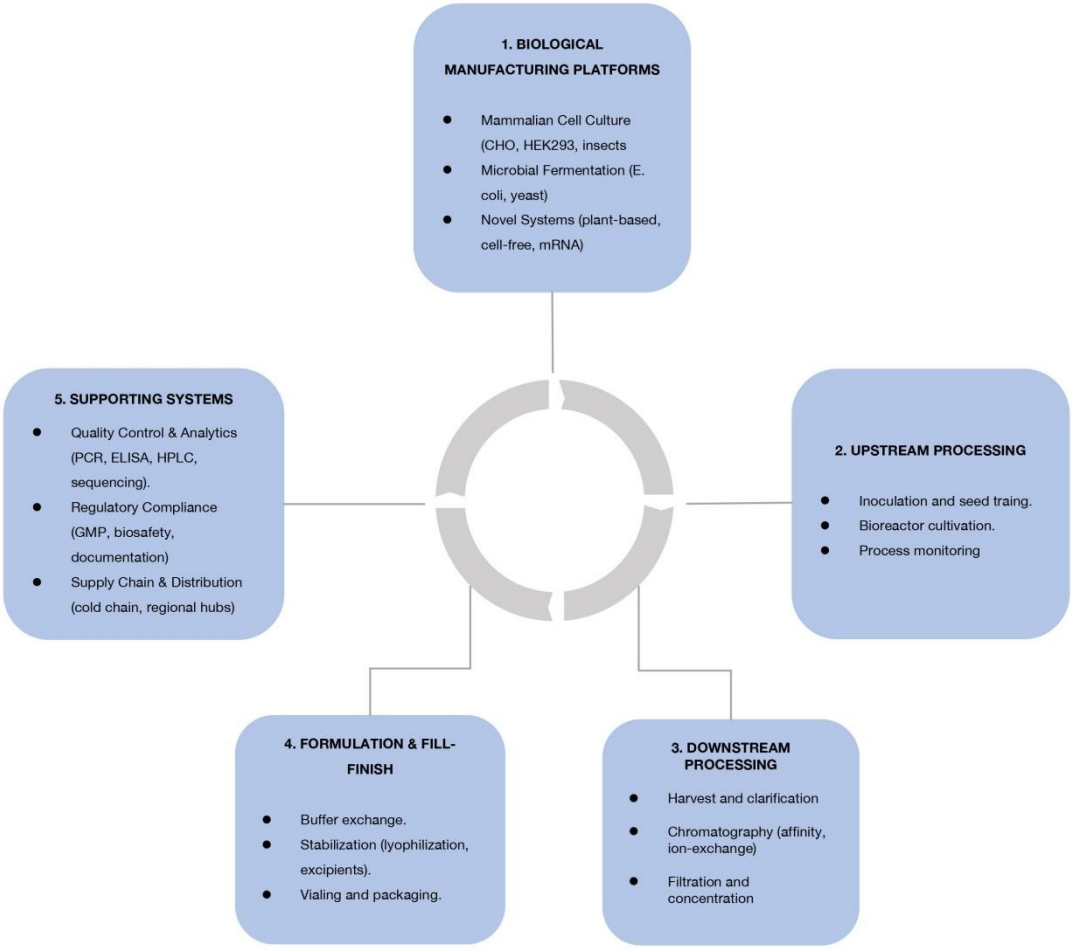

Fig. 1. Overview of biologic manufacturing platforms and production workflows. PCR – polymerase chain reaction; GMP – Good Manufacturing Practice; HPLC – high-pressure liquid chromatography; *E. coli* – *Escherichia coli*; mRNA – messenger ribonucleic acid.

To provide quick clinical and policy guidance, Table I summarizes the principal manufacturing platforms across key dimensions relevant to RLS, including development speed, immunogenicity, thermostability and cold-chain dependence, infrastructure and skill requirements, relative cost, scalability, representative examples, and overall suitability for RLS.

Table I. Comparative summary of vaccine and biologic manufacturing platforms across key dimensions for resource-limited settings

Dimension	Egg-based / cell culture	Recombinant protein	VLP	Viral vector	mRNA	Suitability for RLS
Development speed	Slow; strain adaptation takes months	Moderate to slow	Moderate	Moderate	Very fast (days to weeks)	Speed favours mRNA; near-term feasibility favours protein/VLP

Immunogenicity	Established; often needs boosting	Good; frequently adjuvant-dependent	High; repetitive native antigen display, dose-sparing	High; strong cellular and humoral responses	High; strong responses with LNP delivery	Protein/VLP give durable humoral immunity with simpler logistics
Thermostability / cold chain	2-8°C; moderate	Good (2-8°C)	Good (2-8°C)	Moderate (often frozen)	Poor; requires deep-freeze logistics	Protein/VLP best suited to weak cold chains
Infrastructure / skill demand	Low to moderate; well established	Moderate; can reuse mAb capacity	Moderate to high; assembly and QC intensive	High; complex biosafety	Very high; specialized reagents and equipment	Lower demand favors egg/cell and protein platforms
Relative cost	Low (egg); moderate (cell)	Moderate	Moderate	High	High	High capital cost limits mRNA/viral vector in RLS
Scalability	Limited by egg/cell supply	Good with bioreactors	Good but assembly-sensitive	Good	Rapid but reagent-limited	Protein platforms scale most predictably in RLS
Representative example	Influenza, yellow fever	Hepatitis B, RTS,S malaria	HPV (Gardasil), hepatitis B	Ebola, ChAdOx1 COVID-19	COVID-19 (BNT162b2, mRNA-1273)	Protein/VLP best near-term fit; mRNA aspirational target

VLP – virus-like particles; RLS – resource-limited settings; LNP – liquid nanoparticles; mRNA – messenger ribonucleic acid; QC – quality control; COVID-19 – coronavirus disease 2019; HPV – human papilloma virus

Manufacturing challenges in resource-limited settings

Infrastructure limitations (utilities, biosafety, cold storage)

These three interlocking infrastructural challenges (utilities, biosafety, cold storage) to manufacturing in RLS, where unstable electricity and water supply are the most basic challenges, while biosafety in RLS is extremely limited [37]. A multi-country assessment revealed seven categories of challenges (Table II), ranging from the absence of regulatory frameworks, lack of biosafety awareness, inadequate infrastructure, and insufficient access to equipment, reagents, and maintenance [37].

Cold chain and storage

Over 25% of vaccines are wasted annually globally, with cold chain failures in RLS being a significant contributing factor [38]. A cross-sectional study in Ethiopia showed that only 57.8% of immunization centers had complete temperature records, and most lacked functional cold chain equipment altogether [39]. In Turkana County, Kenya (2022), a survey of 128 health facilities identified significant gaps in vaccine storage and distribution methodologies at the last mile [40]. Due to a lack of sufficient electricity, new technologies can now be applied and include solar-powered refrigeration and Internet of Things (IoT)-based portable vaccine storage modules for last-mile delivery [41].

Supply chain and raw material constraints

The supply chains in RLS are inherently fragile. They are organized along the administrative levels of the government, such as national, regional, and district) and if there is a lack of warehousing, cold chain equipment, transportation, or trained staff in any of these levels, the whole chain collapses [42]. A systematic review conducted by Seidman and Atun [43] revealed that the pharmaceutical supply chains in RLS are characterized by high expenditure shares (high-cost drivers) and inefficient procurement and distribution processes. When it comes to raw material, in many cases of medical devices, it is estimated that 70%–90% of devices in resource-poor environments fail to function after a certain period of time, primarily because they were designed for use in resource-rich environments where electricity and maintenance infrastructure for consumables and spare parts are available [44].

Skilled workforce shortages and training gaps

The core problems (skills mismatch and scarcity), A World Bank study in five African nations (Ghana, Kenya, Zimbabwe, Tanzania, and Zambia) identified that the lack of capability development by manufacturing enterprises is one of the most fundamental constraints to productivity enhancement [45]. The productive structure of Sub-Saharan Africa is marked by low economic complexity and fragmented capabilities, in contrast to East and South Asia [46]. This low complexity is indicative of, and contributes to, the absence of specialized skills in manufacturing. Various initiatives such as Afro Advac, Annual African Vaccinology Course (AAVC) – Cape Town, South Africa, Vaccinology in Africa Course – Nairobi, Kenya, and Vaccinology in Africa Master's Level Courses – rotating between East and West Africa, are some of the training to improve vaccinologists; however, the challenges persist [47].

Financial and market sustainability challenges

A study conducted in 2021, commissioned by the Open Society Foundations, revealed that the funding deficits are not caused by the absence of financial capital in the global market, but instead,

the root causes lie in the market environment [48]. Financial sustainability through business activities depends on the availability of sufficient demand, and the market demand for pharmaceuticals in Africa is fragmented over a large number of small markets with limited purchasing power [48]. Another challenge is dependence on AID from developed countries, as during pandemics (COVID-19), Africa got left behind [49]. Domestic manufacturers face competition from low-priced imports from India and China, where manufacturers enjoy huge economies of scale, supply chains, and sometimes indirect government subsidies [49]. However, simulation analyses indicate that despite higher costs, lack of political will from the African Union's Abuja Declaration (2001), local African pharmaceutical manufacturing need not be expensive or price unaffordable, provided governments can guarantee adequate market access for local manufacturers. Multinational pharmaceutical firms are unwilling to manufacture drugs for diseases in developing countries because of limited purchasing capacity [49]. Drug and vaccine manufacturing in RLS faces a consistent set of interlocking barriers, regulatory, technical, financial, and structural, but recent literature identifies concrete mitigation strategies for each. Table II shows that the seven principal barriers to biologics manufacturing include a weak regulatory framework, substandard Good Manufacturing Practice (GMP) compliance, inadequate infrastructure, limited skilled workforce, capital and financing constraints, small and fragmented markets, and dependence on imported raw materials. The mitigation strategies include harmonizing regional standards and for nations to provide funding for biologics production.

Table II. Key manufacturing barriers and mitigation strategies in resource-limited settings

S/N	Barrier	Description	Mitigation Strategies
1.	Weak regulatory frameworks	Fragmented or under-resourced regulatory bodies; limited capacity for GMP inspections and quality enforcement	Harmonize regional standards (e.g., via WHO prequalification); invest in national regulatory authority capacity building; adopt WHO GMP as a common baseline
2.	Substandard GMP compliance	Manufacturers struggle to meet international GMP standards due to aging facilities, poor documentation practices, and limited quality culture	Phased GMP upgrading programs; international technical assistance and twinning with established manufacturers; WHO-supported GMP training
3.	Inadequate infrastructure	Unreliable electricity, water, transport, and cold chain logistics raise production costs and limit capacity	Public investment in industrial zones with dedicated utilities, regional infrastructure corridors, and renewable energy solutions for manufacturing sites
4.	Limited skilled workforce	Shortage of pharmacists, production engineers, quality assurance specialists, and regulatory scientists	Targeted STEM and pharmaceutical sciences education; diaspora engagement programs; south-south technical cooperation and training exchanges

5.	Capital and financing constraints	High cost of capital, limited access to long-term financing, and unfavorable lending terms discourage investment in manufacturing	Development finance institution lending, tax incentives, and investment guarantees; blended finance models combining public and private capital
6.	Small and fragmented markets	Individual country markets are often too small to achieve economies of scale, making local production uncompetitive against imports	Regional market integration (e.g., through SADC, EAC pooled procurement); harmonized registration to enable cross-border sales
7.	Dependence on imported raw materials	Most RLS import >80% of active pharmaceutical ingredients (APIs) from India and China, creating supply chain vulnerability and cost exposure	Develop regional API manufacturing hubs; invest in continuous flow chemistry for local API synthesis; and strategic stockpiling agreements

WHO – World Health Organization; GMP – Good Manufacturing Practice; STEM – Science, Technology, Engineering, and Mathematics; API – active pharmaceutical ingredient; SADC – Southern African Development Community; EAC – East African Community

Innovations enabling local biologic production

Innovations in biologic and vaccine manufacturing are transforming production in RLS by introducing adaptable, cost-effective technologies and collaborative models that address infrastructure constraints and accelerate access. Modular and flexible facilities stand out, allowing rapid deployment of containerized or re-configurable systems that minimize infrastructure needs and support decentralized operations in RLS [50,51]. These "plug-and-play" designs drastically shorten deployment timelines, from years to months, while supporting decentralized operations and outbreak responses, allowing adaptation to fluctuating demands without massive fixed investments. Single-use and closed-system technologies further boost efficiency and safety by minimizing contamination risks through disposable components that eliminate extensive cleaning and validation [52]. Bioreactors and tubing systems reduce water and energy consumption, vital in water-scarce regions, while streamlining processes for mRNA, viral vector vaccines, or monoclonal antibody production, though end-of-life recycling challenges remain a sustainability concern [53,54]. Digitalization and automation incorporate real-time analytics, AI-driven predictive monitoring, and process analytical technology (PAT) to optimize quality and yields in under-resourced environments, enabling data-driven decisions and reducing human error [55,56]. Public-private partnerships (PPPs) and regional manufacturing hubs amplify these advances, with initiatives like the African Vaccine Manufacturing Accelerator (AVMA) and Partnership for African Vaccine Manufacturing (PAVM) facilitating technology transfer, shared facilities, and capacity building across Africa [57,58,59,60]. While highly promising, successful adoption requires targeted training and local ownership to ensure equitable and sustainable outcomes. Figure 2 shows a modular manufacturing model of vaccine and biological drugs, which is producing vaccines in small, self-contained, standardized production units known as modules (modular upstream unit,

modular downstream unit, modular fill and finish unit). This model is very suitable for RLS as it is flexible, scalable, and has rapid deployment.

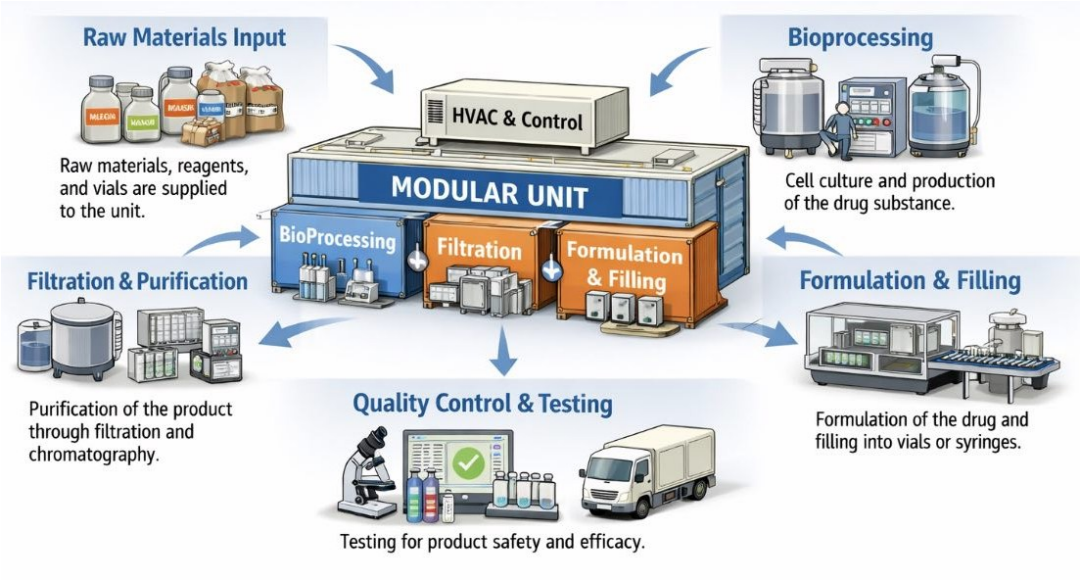

Fig. 2. Modular manufacturing model for vaccines and biologics in resource-limited settings. HVAC – heating, ventilation, and air condition.

Quality control and regulatory considerations

Quality control and regulatory frameworks are foundational and essential to guaranteeing the safety, potency, and consistency of vaccines and biologics produced in RLS, where infrastructure and capacity constraints can compromise standards and delay access. GMP requirements serve as the bedrock, mandating sterile environments, rigorous process validation, traceability, and risk-based controls to prevent contamination and ensure batch-to-batch reliability [61]. In RLS, GMP adaptation often incorporates cost-effective alternatives like the 3Rs (Replacement, Reduction, Refinement) principles to minimize animal testing while maintaining standards of quality, though challenges such as limited clean room facilities and skilled personnel persist, necessitating phased implementation and external support [62]. Quality control testing rigorously assesses safety (e.g., sterility, endotoxin levels), potency (efficacy bio-assays), and consistency (stability and lot uniformity), increasingly leveraging advanced tools like chemo-sensors and real-time contaminant detection to address biologics' inherent variability [56,63]. These methods are essential and enable faster release testing but require affordable, portable solutions suitable for remote or RLS. National Regulatory Authorities (NRAs) and WHO prequalification (PQ) provide essential oversight: Functional NRAs perform inspections, lot release, and post-market surveillance, while PQ facilitates global procurement through bodies like UNICEF and Gavi by verifying compliance with international standards, thereby building trust in LMIC-manufactured products [64,65]. However, weak NRAs can cause delayed approvals, highlighting the need for capacity strengthening. Regulatory harmonization efforts, led by the African Union Development Agency-NEPAD (AUDA-

NEPAD) through the African Medicines Regulatory Harmonization (AMRH) program and the African Medicines Agency (AMA), standardize evaluations across regions like East African Community (EAC), Southern African Development Community (SADC), and Economic Community of West African States (ECOWAS). AUDA-NEPAD coordinates these initiatives in partnership with NRAs, regional economic communities, the African Union (AU) Commission, WHO, and development partners to address fragmented systems, expedite medicine registration, promote reliance mechanisms, reduce duplication, accelerate approvals, and improve access to quality medical products [66,67,68]. Comparable initiatives in Asia (Association of Southeast Asian Nations – ASEAN) and Latin America (Pan American Health Organization – PAHO) offer mutual recognition of models. Despite notable progress, challenges like inconsistent political commitment, funding shortages, countries' capacity disparities, and legislative alignment delays impede full implementation and equitable, sustainable outcomes [69].

DISCUSSION

The urgent global need for vaccines and biologics, especially in RLS, requires a comprehensive strategy to address the specific challenges encountered in these settings. The evidence shows that there is no one-size-fits-all manufacturing platform for all LMIC contexts. Instead, the choice of platform should be based on local capacity, disease targets, and long-term sustainability goals. Egg-based and cell culture systems remain useful because they have well-established protocols, are easier to use, and can work with existing infrastructure [70]. However, their limitations in scalability, speed, and product consistency make them less useful for addressing new health threats [71]. On the other hand, mRNA platforms can quickly adapt to new pathogens; however, they depend on cold chains, special reagents, and LNP formulation, which makes them difficult for most African and Asian manufacturers to acquire immediately without adequate investment in technology transfer and infrastructure [72,73]. Recombinant protein and VLP platforms are a good compromise because they balance thermostability with production feasibility [74,75]. This is especially true when there is already bioprocessing capacity for monoclonal antibodies or therapeutic proteins. A more explicit comparison of these two platforms clarifies why both, rather than either alone, are attractive for RLS. Recombinant protein subunit vaccines are expressed in well-characterised hosts (bacteria, yeast, insect, or mammalian cells), draw on decades of process knowledge directly transferable from the monoclonal-antibody industry, and yield thermostable products compatible with standard 2–8°C cold chains; their principal limitations are comparatively slow antigen-specific process development and a frequent need for potent adjuvants to reach adequate immunogenicity, as exemplified by the adjuvanted hepatitis B vaccine and the RTS,S/AS01 malaria vaccine [74]. VLP platforms, by contrast, present repetitive, conformationally

native antigen arrays that elicit strong, durable, dose-sparing B-cell responses and have an established manufacturing and licensure record in the hepatitis B (recombinant HBsAg particles) and HPV (Gardasil, Cervarix) vaccines, both produced at scale in yeast or insect-cell systems well matched to decentralised production [75]. The principal trade-off is that correct self-assembly, particle integrity, and reproducible purification are more technically demanding and yield-sensitive than soluble protein production, requiring tighter in-process analytics and quality control. Considered together, recombinant protein platforms offer manufacturing simplicity and a lower analytical burden, whereas VLPs offer superior intrinsic immunogenicity and antigen dose-sparing; because both depend on the same upstream expression infrastructure, the most realistic pathway for many RLS is to establish recombinant subunit capacity first and to extend it to VLP production as analytical and quality-control capabilities mature. This staged, shared-infrastructure logic is the practical conclusion we wish readers to draw from the cross-platform comparison summarized in Table I. The review, on the other hand, makes it clear that technological innovation is not enough on its own. Modular facilities, single-use systems, and digital process automation are the most promising new technologies [76]. However, they have only been effective when combined with strong regulatory harmonization, such as WHO PQ, and long-term market mechanisms that deal with fragmented demand and competition from imports [77]. The ongoing dependence on imported raw materials, particularly active pharmaceutical ingredients (APIs) from India and China, signifies a structural vulnerability that regional manufacturing hubs and PPPs must urgently rectify. To gain fair access, we need to go beyond pilot projects and make coordinated investments in training the workforce, making regulations more similar across regions, and using blended finance models that lower the risk of local production while still making it affordable and high-quality. Without these supportive conditions, even the most cutting-edge platforms may not be accessible to the people who need them. Financial sustainability remains a significant barrier to the establishment of thriving local manufacturing ecosystems. The fragmented nature of pharmaceutical markets in Africa, compounded by competition from low-cost imports, creates an environment where local production struggles to compete. To address these issues, it is crucial to develop innovative financing mechanisms that can support local manufacturers, such as blended finance models and development finance institution lending [78]. PPPs can play a transformative role in mobilizing resources and fostering collaboration between stakeholders [79]. By leveraging the strengths of both sectors, these partnerships can facilitate technology transfer, shared facilities, and capacity-building initiatives that enhance local production capabilities. Looking forward, decentralized and platform-based manufacturing ecosystems represent a promising pathway. Modular facilities, single-use technologies, and digitalized production systems can enable flexible,

scalable, and cost-efficient manufacturing tailored to LMIC contexts. Such systems, coupled with regional collaboration, have the potential to transform global biologics production into a more equitable and responsive model.

Clinical, veterinary, and public health implications

Increasing the ability of RLS to make vaccines and biologics locally will have a huge impact on public health, clinical care, and veterinary health systems. One of the most immediate benefits ensures better access to important vaccines and biologic therapies for the population in general. This will make them less reliant on imports and help prevent supply disruptions. This is especially important for diseases that are common in certain areas, like malaria, TB, and NTDs, where getting vaccines quickly can greatly lower the number of people who get sick or die. Producing vaccines locally is a key to strengthening routine immunisation programs, which is important for long-term public health. By ensuring a consistent and reliable supply of vaccines, healthcare systems can maintain high immunization rates, particularly among vulnerable populations. Furthermore, local manufacturing capabilities enable a swift response to emerging infectious diseases, allowing for rapid vaccine deployment during outbreaks. This quickness is vital for mitigating the impact of epidemics and enhancing public health preparedness. The implications extend beyond human health; strengthening local production of veterinary biologics is crucial for food security and animal health. As the demand for animal-sourced foods continues to rise, ensuring the health of livestock through effective vaccination programs is essential for sustaining agricultural productivity. Local manufacturing of veterinary vaccines can help prevent disease outbreaks that threaten animal populations and, by extension, food supply chains. This can lead to improved food security and economic stability in resource-limited regions. Table III shows a comparison of imported vaccines vs locally manufactured biologics. The comparisons are made focusing particular emphasis on cost, supply chain, regulatory oversight, responsiveness to outbreaks, cold chain dependence, supply reliability, economic impact, and quality control.

Table III. Comparison of imported vs locally manufactured biologics

S/N	Parameter	Imported Biologics	Locally Manufactured Biologics	References
1.	Cost	Higher due to tariffs/shipping	Lower due to reduced transportation	[80]
2.	Supply chain lead time	3–12 months	1–3 months	[81]
3.	Regulatory oversight	FDA and WHO-prequalified, with limited local control	Under local NRA (requires capacity building)	[82,83]
4.	Responsiveness to outbreaks	Delayed due to export bans and allocation	Rapid adaptation to local strains	[83]

5.	Cold chain dependence	High (often -70ºC to -20ºC)	Can be optimized for thermostability	[84,85]
6.	Supply reliability	Vulnerable to global demand shocks	More predictable with regional stockpiles	[85]
7.	Economic impact	Limited local benefit	Supports the local economy	[80]
8.	Quality control	Varies by country of origin	More tailored to local standards	[86]

FDA – Food and Drug Authority; WHO – World Health Organization; NRA – National Regulatory Authority

Policy recommendations and capacity building

Achieving sustainable vaccine and biologifcs manufacturing in RLS, requires coordinated policy interventions and strategic investments. Governments and international organizations should prioritize funding for the development of state-of-the-art manufacturing facilities that adhere to GMP standards. Investments should focus on modular systems that can be rapidly deployed and adapted to meet changing health needs. By establishing dedicated industrial zones with reliable utilities, countries can create an environment conducive to sustainable biologics production. Technology transfer remains a cornerstone of capacity building [87]. However, effective transfer extends beyond physical infrastructure to include knowledge exchange, process optimization, and regulatory alignment. Intellectual property (IP) frameworks must strike a balance between incentivizing innovation and enabling equitable access. Voluntary licensing, patent pooling, and global initiatives can facilitate broader access to critical technologies while maintaining innovation incentives. Collaborations between multinational pharmaceutical companies and local entities can foster innovation and enhance production capabilities [88]. Building a skilled workforce is vital for the success of local manufacturing initiatives. Governments should invest in workforce development programs that focus on training personnel in key areas such as vaccine production, quality assurance, and regulatory compliance. Establishing regional training centres that offer specialized courses in vaccinology and biomanufacturing can help bridge the skills gap. Engaging local universities and research institutions in these initiatives will further strengthen the educational framework. Additionally, enhancing regional collaboration is essential for overcoming the fragmented nature of pharmaceutical markets in RLS. Policymakers should promote regional procurement mechanisms that allow countries to pool resources and collectively negotiate for bulk purchases, thereby achieving economies of scale. Initiatives such as the AVMA can facilitate collaborative efforts in technology sharing and capacity building, ensuring that all member states benefit from improved access to vaccines and biologics [89]. By implementing these policy recommendations, RLS can create a sustainable framework for local vaccine and biologic production, ultimately improving public health outcomes.

CONCLUSIONS

This review addressed the challenges, innovations, and pathways to sustainable access in manufacturing platforms for vaccines and biological drugs in LRS. Key findings reveal that LRS such as Africa are in need of vaccines and biological drugs due to increased disease burden such as TB, HIV/AIDS, malaria, NTDs, emerging, and reemerging infectious diseases. There are a lot of challenges in most LRS, such as Africa, which produce only about 1% of the global vaccine supply chain. The challenges which include reduced supply chain, systemic limitations to infrastructure, lack of specialized workforce, security challenges, inadequate cold chain, lack of political will, reduced funding, technology transfer issues, legislative alignment delays hindering full implementation and equitable sustainable outcomes. This review acknowledges that it was conducted as a narrative review. Narrative reviews particularly lack a systematic, and reproducible methodology which often lead to selection bias in the inclusion of the studies. This review lacked a formal quality appraisal of included studies, resulting in the incorporation of studies that vary in methodological rigor being discussed without a structured assessment. There are new technologies such as modular facilities, single-use systems, and digital process automation. They have both pros and cons in LRS, however, they can be deployed scalable and flexible, and can be deployed rapidly in these zones, reducing the dependence on imports and delays in pandemic scenarios, as shown during the COVID-19 global pandemic. Building on these findings, we propose a prioritized research agenda to move from description toward implementation. First, head-to-head techno-economic and life-cycle analyses are needed to quantify the real cost of goods, achievable yield, and environmental footprint of competing platforms (egg-based, cell-culture, recombinant protein, VLP, viral-vector, and mRNA) under realistic LRS operating conditions, so that platform selection rests on local evidence rather than assumption. Second, implementation-science studies should evaluate how modular, single-use, and digitally automated facilities perform where utilities are intermittent, including the development and field validation of thermostable and lyophilised formulations that reduce cold-chain dependence. Third, regulatory-science research should measure how harmonisation mechanisms the AMA, reliance pathways, and WHO PQ affect registration timelines and product quality, building the evidence base for continent-wide regulatory strengthening. Fourth, health-economic and market-shaping studies should test financing and demand-pooling instruments, such as blended finance, advance purchase commitments, and pooled procurement, to identify which models most effectively de-risk sustainable local production against fragmented demand. Fifth, workforce and knowledge-transfer research should determine which training, twinning, and south-south cooperation models most rapidly close the biomanufacturing skills gap. Finally, future systematic reviews incorporating

formal quality appraisal would complement and validate the present narrative synthesis. In conclusion, for the manufacturing of vaccines in LRS, governments should be committed to offering change, supporting people with relevant skills by providing facilities, or funding for research, capacity building initiatives, and upscaling their work.

Abbreviations

AAVC	Annual African Vaccinology Course
AIDS	acquired immunodeficiency syndrome
AMA	African Medicines Agency
AMRH	African Medicines Regulatory Harmonization
API	active pharmaceutical ingredient
ASEAN	Association of Southeast Asian Nations
AUDA	African Union Development Agency
AVMA	African Vaccine Manufacturing Accelerator
BRICS	Brazil, Russia, India, China, South Africa
CEPI	Coalition for Epidemic Preparedness Innovations
COVAX	COVID-19 Vaccines Global Access Facility
COVID-19	coronavirus disease 2019
EAC	East African Community
ECOWAS	Economic Community of West African States
FDA	Food and Drug Authority
Gavi	Global Alliance for Vaccines and Immunization
GMP	Good Manufacturing Practice
HBV	hepatitis B virus
HIV	human immunodeficiency virus
HPLC	high-pressure liquid chromatography
HPV	human papilloma virus
IBDV	infectious bursal disease virus
IoT	Internet of Things
IP	intellectual property
LMICs	low- and middle-income countries
LNP	lipid Nanoparticles
mRNA	messenger ribonucleic acid
NEPAD	New Partnership for Africa’s Development

NRA National Regulatory Authority

NTDs neglected tropical diseases

PAHO Pan American Health Organization

PAT process analytical technology

PAVM Partnership for African Vaccine Manufacturing

PCR polymerase chain reaction

PPP public-private partnership

PQ prequalification (WHO PQ system)

RLS resource-limited settings

RSV respiratory syncytial virus

SADC Southern African Development Community

STEM Science, Technology, Engineering, and Mathematics

TB tuberculosis

VLPs virus-like particles

WHO World Health Organization

Conflict of interest

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