Vaccines for all? Opportunities and challenges for vaccine-related technology transfers to LMICs

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Abstract

The lack of timely access to Covid-19 vaccines played a significant role in low- and middle-income countries (LMICs) being disproportionately affected by the Covid-19 pandemic. Vaccine manufacturing is highly concentrated in a few geographical regions, dominated by a small number of manufacturers, and focussed on specific diseases. To increase resilience for future disease outbreaks and pandemics, and ensure global health security and equity, it is necessary to build vaccine manufacturing capacity in LMICs and to facilitate technology transfer activities.

Conducting successful technology transfer - where the knowledge and ability to carry out a manufacturing process is shared from an originator to a secondary user - is critical to increasing global vaccine manufacturing capacity. However, it is intertwined with a broader set of structural challenges and barriers. This policy brief summarises the findings from a review of the academic and grey literature, and stakeholder interviews on the barriers, enablers and potential policy solutions related to bringing innovative vaccine solutions to and building local manufacturing capacity in LMICs. It highlights the biggest challenges related to technology transfer, which include costs and upfront capital requirements, manufacturing know-how and a skilled workforce, access to innovative technologies and technology platforms, regulatory maturity, knowledge systems, and infrastructure capabilities. It also maps existing initiatives that help address some of these challenges and provides policy recommendations to enable further progress.

Introduction

Unequal access to Covid-19 vaccines resulted in a higher proportional death toll and prolonged the pandemic in LMICs by giving the virus the opportunity to spread and mutate [2]. To increase resilience and prepare for future disease outbreaks and pandemics, and to achieve global health security, equity and drive progress towards the Sustainable Development Goals (SDGs), it is necessary to accelerate the development, manufacture, and distribution of vaccines worldwide [3,4, 9]. Immunisation plays a key role in achieving 14 of the 17 SDGs and it is closely aligned with the SDG transformative promise to 'leave no one behind' as articulated by the Immunization Agenda 2030 (IA2030) [9,10]. An essential part of vaccine equity is sufficient local vaccine manufacturing capacity. Local productive capacity also benefits countries' economies in the long-term, by nurturing expertise and creating quality jobs in LMICs, which in turn contributes to structural transformation, economic growth, and pandemic preparedness [5, 6].

In 2022 and 2023, the Future Vaccine Manufacturing Research Hub (the 'Vax-Hub') carried out interviews[1] and a literature review on the barriers, enablers and potential policy solutions related to bringing innovative vaccine solutions to and building local manufacturing capacity in LMICs.

The Vax-Hub was a five-year academic collaboration (2018-2023) led by UCL Biochemical Engineering and the University of Oxford and funded by the UK's Department of Health and Social Care's (DHSC) Official Development Assistance programme, the UK Vaccine Network. The Vax-Hub's mission is to secure the supply of essential vaccines to low- and middle-income countries. Building on the success of the 2018-2023 Vax-Hub, two new vaccine hubs were awarded research funding in 2023 - Manufacturing Research Hub for a Sustainable Future (Vax-Hub Sustainable) and the Vaccines Manufacturing Hub for LMICs (Vax-Hub) Global. Vax-Hub Global aims to enhance future vaccine manufacturing by delivering flexible, easily transferable vaccine platform technologies and simplified engineering solutions to enable the development of low-cost, effective, and globally deployable vaccines to LMICs. Vax-Hub Sustainable focuses on the UK end-to-end vaccine research and manufacture and it is also exploring how to incorporate sustainability principles and practices into vaccine manufacturing.

[1] Vax-Hub conducted 21 scoping meetings and interviews with stakeholders from organisations in academia (n=3), the Vax-Hub user group (n=3), UK policy (3), the United Nations (2), and international organisations (n=7).

Context

Although there is a growing number of manufacturers globally that are involved in all steps of vaccine manufacturing, the vaccine manufacturing and distribution market is highly concentrated in a few geographical regions, as illustrated in the tables below [7]. Many global suppliers are only able to produce a few vaccines and tend to only provide vaccines for local markets [7].

Figure 1. Regional vaccine volume distribution versus supply – with COVID-19 (in %)

	Distributed in:					
Supplier	Africa	Americas	Eastern Mediterranean	Europe	South-East Asia	Western Pacific
Africa	0	0	0	0	0	0
Americas	17	57	26	56	61	15
Eastern Mediterranean	0	0	0	0	0	0
Europe	25	29	23	39	2	6
South-East Asia	43	6	27	2	79	1
Western Pacific	14	8	17	4	13	78
TOTAL	**100**	**100**	**100**	**100**	**100**	**100**

Source: WHO 2022

Figure 2. Regional vaccine volume distribution versus supply – without COVID-19 (in %)

	Distributed in:					
Supplier:	Africa	Americas	Eastern Mediterranean	Europe	South-East Asia	Western Pacific
Africa	1	0	0	0	0	0
Americas	7	31	9	11	1	5
Eastern Mediterranean	0	0	4	0	0	0
Europe	26	39	26	76	3	5
South-East Asia	57	21	56	6	93	5
Western Pacific	9	8	4	7	3	85
TOTAL	**100**	**100**	**100**	**100**	**100**	**100**

Source: WHO 2022

Conducting successful technology transfer, where the knowledge and ability to carry out a manufacturing process is shared from an originator to a secondary user [5, 7], is critical to increasing global vaccine manufacturing capacity. This enables countries to acquire the knowledge, experience, and equipment necessary for advanced and innovative industrial products and processes [11].

Addressing challenges related to technology transfer.

Costs and upfront capital requirements

There is a need for long-term coordinated financing and procurement mechanisms, large public and private investments, official development assistance, and to create funds and facilities for funding that can be mobilised quickly [5, 7, 12, 13]. Many LMICs lack the capital that is necessary to start a commercial vaccine manufacturing plant and to meet requirements for drug safety, quality and efficacy, and good manufacturing practices (GMP), whilst also considering the operational costs [4, 7, 14].

Interviews confirmed the cost challenges in the manufacturing of vaccines. The ability to create the business case for vaccine manufacturing and to predict long-term demand for vaccines are key challenges, as well as the price sensitivity of key global health actors[2], which makes it difficult for LMICs to enter global markets.

Know-how and a skilled workforce

Lacking manufacturing know-how and a skilled workforce creates barriers to vaccine manufacturing across the entire value chain [5, 6, 7, 8]. Concerted efforts are necessary to train a new multi-disciplinary and permanent workforce with knowledge that is scientific, technical, regulatory, and product-specific for manufacturing, GMP, and quality control systems [4, 6, 14].

Interviewees noted that there should be a mix of training that invites researchers and industry stakeholders to countries with already established vaccine manufacturing capabilities and to run training initiatives in LMICs and regions, for example by training the trainers. Training programmes should focus on areas that include collaboration in developing technologies and products, and building capabilities across the whole downstream and upstream of vaccine manufacturing, whilst also considering the development of common evaluation frameworks.

Access to technologies and technology platforms

There needs to be an increased focus on vaccine platform technologies[3] [26], whereby vaccines for different diseases are delivered within a single system. Innovative vaccine platform technologies can offer

[2] Key global health actors cost vaccines at a price that is not much higher than that of manufacturing.

[3] Vaccine platform technologies refers to where a single delivery system, for example a viral vector, is developed that can be modified to produce vaccines against a number of different pathogens.

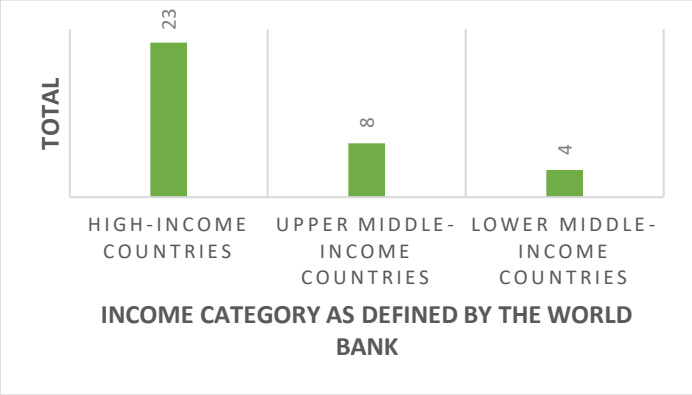
acceleration, flexibility, and pandemic readiness [15, 16].

Interviewees highlighted the importance of building technology capabilities in inter-pandemic contexts that can be applied in the case of a pandemic and noted that they would prioritise mRNA[4] [25] and viral vectors, as vaccine technologies with high potential.[5] [23]

Regulatory maturity

Strong regulatory systems are required across the entire vaccine life cycle and should be streamlined to facilitate investment [4, 5, 6, 7, 8]. National regulatory systems that have reached regulatory maturity levels, as defined by the WHO [17] are concentrated in High Income Countries (HICs). Interviewees highlighted that training is an important tool for building the capabilities necessary to reach regulatory maturity at a national level. However, for any measure to be successful, it is necessary with WHO pre-qualification[6] so that LMICs can sell to the Gavi the Vaccine Alliance and UNICEF, as well as other countries.

Figure 3. Vaccine producing countries with maturity level 3 or 4 in national regulatory systems (N=35)



Source: WHO 2022

Infrastructure capabilities

Hard infrastructure challenges for vaccine manufacturing include water quality, availability of services and spare parts, uninterrupted electricity supply, communication and transport networks, and access to ports [7, 8]. Soft infrastructure challenges relate to laws and regulations, norms, and cultures that impact trust and social capital, competition and tariff policy, regulations and regulatory frameworks, and standards [8]. Together, these challenges increase the cost of vaccine manufacturing. Interviewees highlighted the importance of investing in and building the necessary infrastructure in LMICs.

Knowledge systems

Knowledge systems, particularly related to research and development (R&D) and real-time monitoring and data sharing, create a conducive environment for building vaccine capabilities across the entire vaccine value chain and facilitates technology transfer deals between local industry and international partners [8, 13, 15, 18]. However, in some LMICs, investment in research systems accounts for less than 0.5% of GDP due to competition with other government priorities [18]. Interviewees underlined the need to strengthen R&D systems in LMICs and highlighted as an example that much of the research in universities on the African continent tends to be blue skies and long-term, but that manufacturing capabilities also need to be developed.

Collaboration and common goals

It is necessary to promote collaboration underpinned by a human-rights based approach among stakeholders from government, academia, industry, civil society, and philanthropic organisations [1, 8, 13, 15, 28]. Interviewees felt that work needs to be done at the national, regional, and global level to facilitate collaboration and highlighted the importance of information-sharing across initiatives. There is a need for simultaneous and coherent support in market demand, skills, infrastructure, and regulation, which requires extraordinary levels of coordination between a wide array of different stakeholders, coordination which in turn requires strong political commitment both domestically and internationally. Regional collaboration is especially conducive to reducing costs[7] [4,6].

[4] Cells use DNA as a template to make messenger RNA (mRNA) molecules, which are then translated to build proteins. An RNA vaccine consists of an mRNA strand that codes for a disease- specific antigen. The mRNA strand is delivered to the body's cells which use the genetic information to produce the vaccine.

[5] For example, in June 2021, the WHO announced the mRNA vaccine technology transfer hub located in Cape Town, South Africa. The objective of the hub is to build capacity in low-and-middle income countries to produce mRNA vaccines through a centre of excellence and training (the mRNA vaccine technology hub).

[6] WHO pre-qualification is critical to manufacture and sell vaccines at lower volumes and to make vaccine manufacturing cost-effective.

[7] Examples include the Partnership for African Vaccine Manufacturing (PAVM). PAVM aims to enable the African vaccine manufacturing industry to "develop, produce and supply over 60 percent of the total vaccine doses required on the continent by 2040".

Whilst COVID-19 provided an impetus for a growth of different initiatives[8] [6, 19, 20, 21, 22, 24], they are often not coordinated. Evidence has shown that a long-term vision and coherence across industrial, trade and health policies are key factors in successfully developing local manufacturing capacity [27]. Interviewees highlighted the importance of creating common goals and policy objectives through collaborations between the scientific and policy community. To achieve policy coherence, they noted that public health considerations need to be linked with vaccine manufacturing. One interviewee highlighted the importance of having a national leader to facilitate these conversations, such as a public health authority. They also noted the misalignment between global and national health priorities, and that certain diseases (such as tropical diseases) might be less prioritised by the global health community. Greater alignment can be achieved by ensuring that LMICs are represented in global policy fora. Assessments of needs, investments, and the viability of initiatives at national and global levels are also required [13].

Wider governance issues

It is necessary to situate technical solutions within the wider policy landscape related to vaccine manufacturing [5, 7, 8, 12]. Some of the governance issues that have been addressed by other stakeholders include:

- Industrial expertise and resource, as well as industrial policy.
- Global trade and tariff regimes, intellectual property rights systems, global regulatory capacity, and the need to harmonise medicines procurement [6, 12, 13].
- National challenges relate to transparency, favourable economic and policy environments, institutions and practices, as well as political will and stability [5, 6, 7, 8, 12, 13, 15].

Policy recommendations

- Coordinated financing and procurement mechanisms can address the capital requirements for vaccine manufacturing in LMICs. Vaccine manufacturing needs to be feasible from a business perspective and ensure sustainable financing that recognises the long-term funding requirements for vaccine manufacturing.
- Training and skills programmes are necessary across the vaccine development value chain and to build regulatory maturity. Initiatives need to be coherent, well-curated, and require common criteria for what good looks like.
- There should be a broad focus on technologies and technology platforms to adequately prepare for future disease outbreaks.
- Strong regulatory systems are required across the entire vaccine life cycle. Regulatory training can contribute to the strengthening of national regulatory systems.
- Investments are needed to solve both hard and soft infrastructure challenges.
- It is necessary to strengthen research and development in LMICs, including for long-term and blue skies research, as well as practical and basic scientific knowledge.
- Collaboration should be promoted among diverse stakeholders from government, academia, industry, civil society, and philanthropic organisations. Work needs to be done at the national, regional, and global level to facilitate collaboration, information-sharing, and to set common policy goals and objectives.

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References

[1] United Nations General Assembly, Human Rights Council Fifty-third session. 2023. 'Compendium of good practices on access to medicines, vaccines and other health products in the context of the right of everyone to the enjoyment of the highest attainable standard of physical and mental health'. Available at: https://documents.un.org/doc/undoc/gen/g23/069/14/pdf/g2306914.pdf?token=iHA2Mb1gGzqTT4oW92&fe=true

[2] Wellcome n.d. 'What we do: Infectious Disease.' Wellcome, n.d.: https://wellcome.org/what-we-do/infectious-disease

[3] CEPI. 2022. Enabling Equitable Access to COVID-19 vaccines. CEPI, February 2022: https://cepi.net/wp-content/uploads/2020/12/Enabling-equitable-

[8] Other initiatives include the creation of new vaccine manufacturing plants, investments from development finance institutions and multilateral development banks, bilateral support, regional partnerships, technology transfer hubs, training hubs, and COVAX task forces.

access-to-COVID19-vaccines-v8-14-February-2022.pdf

[4] Kumraj et al. 2021. 'Capacity Building for Vaccine Manufacturing Across Developing CountriesThe Way Forward', Hum Vaccin Immunother 18(1): https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8986212/

[5] Zhan, J. 2020. 'Ten Actions to boost low- and middle-income countries' productive capacity for medicines. UNCTAD 27 May 2020: https://unctad.org/news/ten-actions-boost-low-and-middle-income-countries-productive-capacity-medicines

[6] Partnership for African Vaccine Manufacturing. 2022. Framework for Action. PAVM, 2022: https://africacdc.org/download/partnerships-for-african-vaccine-manufacturing-pavm-framework-for-action/

[7] WHO. 2022. Global Vaccine Market Report 2022: A shared understanding for equitable access to vaccines. WHO, November 2022: https://cdn.who.int/media/docs/default-source/immunization/vaccine_access_market/global-vaccine-market-report-2022-template-final2.pdf?sfvrsn=5e8ddbed_6&download=true

[8] Banda et al. 2022. The Localisation of Medical Manufacturing in Africa. The Institute of Economic Justice: The Localisation of Medical Manufacturing in Africa (LoMMiA) project, November 2022: https://www.iej.org.za/wp-content/uploads/2022/11/IEJ-LoMMiA-report_Nov2022.pdf

[9] WHO. 2020. Immunization Agenda 2030: A Global Strategy to Leave No One Behind. WHO, April 2020: https://cdn.who.int/media/docs/default-source/immunization/strategy/ia2030/ia2030-draft-4-wha_b8850379-1fce-4847-bfd1-5d2c9d9e32f8.pdf?sfvrsn=5389656e_69&download=true

[10] Gavi. 2019. Immunisation and the Sustainable Development Goals. Gavi, September 2019: https://www.gavi.org/sites/default/files/document/2019/Immunisation%20and%20the%20SDGs%20%281%29.pdf

[11] UNCTAD. 2021. Technology and Innovation Report 2021: Catching technological waves, Innovation with Equity. UNCTAD, 2021: https://unctad.org/system/files/official-document/tir2020_en.pdf

[12] International Federation of Pharmaceutical Manufacturers and Associations. 2021. Technology Transfer: a collaborative approach to improve global health. IFPMA, 2021: https://ifpma.org/wp-content/uploads/2021/12/IFPMA_Tech-Transfer_A-collaborative-approach-to-improve-global-health_Position-Paper.pdf

[13] Glassman et. Al. 2022. Rapid and Equitable Access to Medical Countermeasures: Lessons, Landscape and Near-term Recommendations. Center for Global Development, May 2022: https://www.ccgdev.org/publication/rapid-and-equitable-access-medical-countermeasures-lessons-landscape-and-near-term

[14] Carmichael, P. 2022. Policy brief: The Skills Agenda for Vaccine Manufacturing. Vax-Hub, July 2022: https://www.ucl.ac.uk/steapp/sites/steapp/files/the_skills_agenda_for_vaccine_manufacturing_vax-hub_workshop_report_jul_2022.pdf

[15] Jensen, N., Barry, A. & A.H. Kelly. 2022. 'More-than-national and less-than global: The biochemical infrastructure of vaccine manufacturing.' Economy and Society 52(1).

[16] CEPI. 2022. Delivering Pandemic Vaccines in 100 Days. CEPI, November 2022: https://cepi.net/wp-content/uploads/2022/11/CEPI-100-Days-Report-Digital-Version_29-11-22.pdf

[17] WHO. 2022. List of National Regulatory Authorities (NRAs) operating at maturity level 3 (ML3) and maturity level 4 (ML4) (as benchmarked against WHO Global Benchmarking Tool. WHO, November 2022: https://cdn.who.int/media/docs/default-source/medicines/regulatory-systems/list-of-nras-operating-at-ml3-and-ml4.v2.pdf?sfvrsn=ee93064f_3&download=true

[18] Drake, T., Fosci, M., Loffreda, L., Velten, L. & R. Johnson. 2019. Research Capacity Strengthening in LMICs: A Rapid Evidence Assessment. Research Consulting, UKAid, & Heart, 2019: https://assets.publishing.service.gov.uk/media/5d42be4eed915d09d8945db9/SRIA_-_REA_final__Dec_2019_Heart___003_.pdf

[19] Xinhua. 2022. 'Botswana launches Covid-19 vaccine manufacturing plant.' XinhuaNet, 29 March 2022: https://english.news.cn/africa/20220330/72d438e82caa4b88a5d3a78ebdbe0b50/c.html

[20] DFC: U.S. International Development Finance Corporation. 2021. 'DFC, IFC, Proparco, and DEG Support South African COVID-19 Vaccine Maker, Aspen.' DFC, June 2023: https://www.dfc.gov/media/press-releases/dfc-ifc-proparco-and-deg-support-south-african-covid-19-vaccine-maker-aspen

[21] European Commission. 2021. 'Republic of Senegal and Team Europe agree to build a manufacturing plant to produce vaccines against COVID-19 and other endemic diseases.' European Commission, 9 July 2021: https://ec.europa.eu/commission/presscorner/detail/en/IP_21_3562

[22] WHO. 2023. 'The mRNA vaccine technology transfer hub.' WHO, 2023: https://www.who.int/initiatives/the-mrna-vaccine-technology-transfer-hub

[23] WHO. 2022. 'Moving forward on goal to boost local production, WHO establishes global manufacturing training hub in Republic of Korea: Bangladesh, Indonesia, Pakistan, Serbia and Viet Nam to receive mRNA technology from the technology transfer hub.' WHO, 23 February 2022: https://www.who.int/news/item/23-02-2022-moving-forward-on-goal-to-boost-local-pharmaceutical-production-who-establishes-global-biomanufacturing-training-hub-in-republic-of-korea

[24] Gavi. 2021. 'COVAX Manufacturing Task Force to tackle vaccine supply challenges.' Gavi, 14 May 2021: https://www.gavi.org/vaccineswork/covax-manufacturing-task-force-tackle-vaccine-supply-challenges

[25] Carmichael, P. 2020. Policy brief: Developing New Vaccines for Pandemics. Vax-Hub, October 2020: https://www.ucl.ac.uk/steapp/sites/steapp/files/vax-hub_vaccine_explainer_part_1_developing_new_vaccines_for_pandemics_oct_2020.pdf

[26] Carmichael, P. 2020. Policy brief: Manufacturing New Vaccines for Pandemics. Vax-Hub, October 2020: https://www.ucl.ac.uk/steapp/sites/steapp/files/vax-hub_vaccine_explainer_part_2_manufacturing_new_vaccines_for_pandemics_oct_2020.pdf

[27] WHO. 2011. 'Local Production for Access to Medical Products Developing a Framework to Improve Public Health'. WHO, 2011: https://cdn.who.int/media/docs/default-source/medicines/local-production/local_production_policy_brief.pdf?sfvrsn=e4485e87_1&download=true