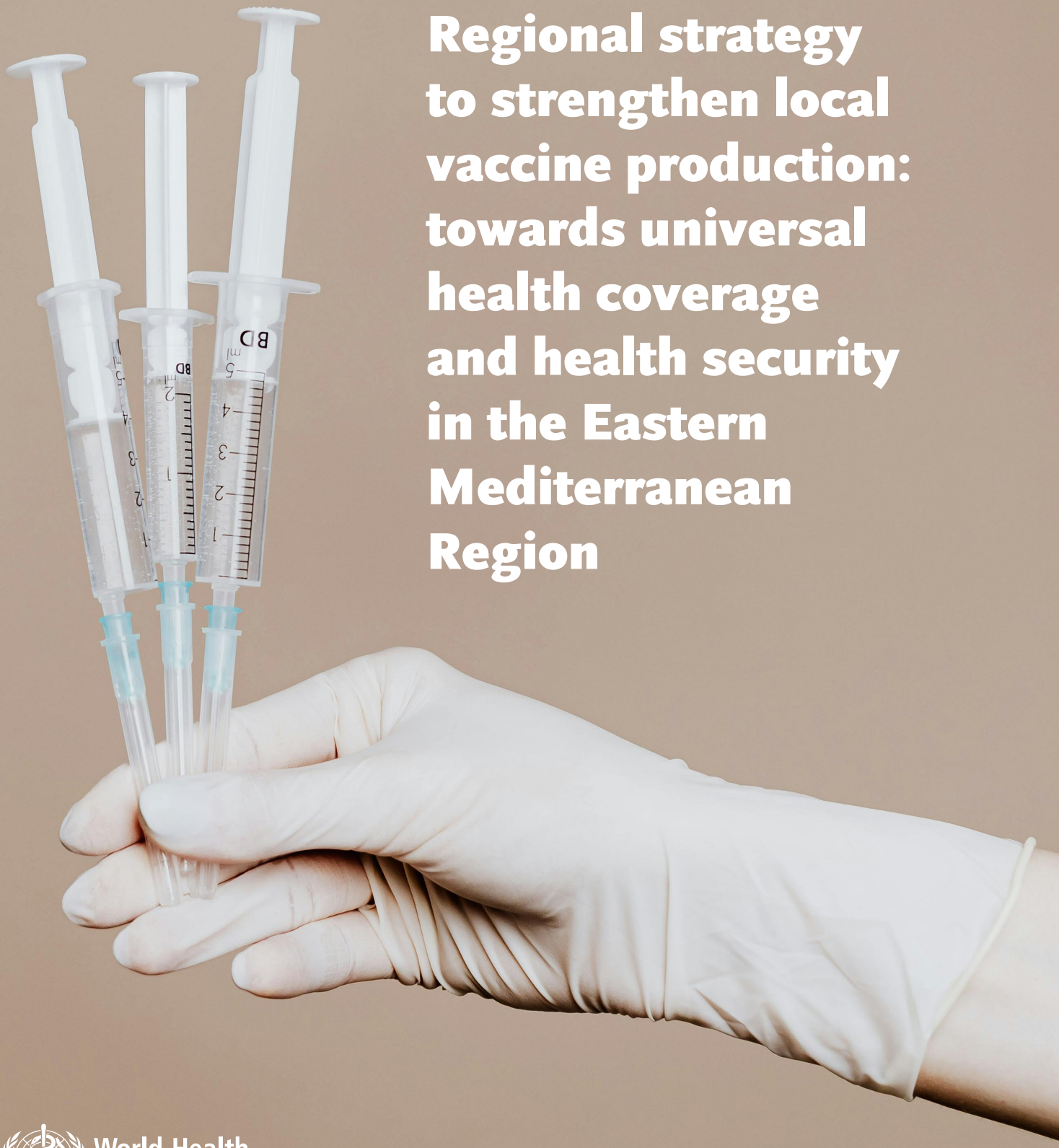
Regional Committee version
October 2024

Regional strategy to strengthen local vaccine production: towards universal health coverage and health security in the Eastern Mediterranean Region



World Health Organization
Eastern Mediterranean Region

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Executive summary

The World Health Organization (WHO) seeks to strengthen the local production of vaccines and other health products to ensure equitable and affordable access to these products to address public health needs for routine immunization and respond to health emergencies.

In the WHO Eastern Mediterranean Region, four vaccine-producing countries, namely Egypt, Islamic Republic of Iran, Pakistan and Tunisia, currently manufacture traditional vaccines for the Expanded Programme on Immunization (EPI). These countries are interested in expanding their vaccine production portfolio to other priority vaccines, such as human papillomavirus, meningococcal, pneumococcal and rabies vaccines, and are considering production of other newly developed vaccines.

Beyond the existing vaccine-producing countries, Morocco, Saudi Arabia and the United Arab Emirates all have active projects in development and are investing in EPI vaccine manufacturing.

During the COVID-19 pandemic, vaccine production capacity increased in the Region, with a special focus on COVID-19 vaccines. Eight pharmaceutical companies in four countries of the Region (Egypt, Islamic Republic of Iran, Pakistan and the United Arab Emirates) manufactured COVID-19 vaccines. However, most of these countries imported vaccines in bulk and performed "fill and finish" pharmaceutical operations.

To prepare countries to respond to future outbreaks and pandemics, and ensure more efficient production of potential future vaccines, WHO is supporting countries to obtain mRNA technology. This technology can be used not only to manufacture COVID-19 vaccine but also other types of vaccines and other biological products to prevent other diseases. So far, 15 manufacturers from the six regions of WHO have been selected to receive mRNA technology transfer, including three manufacturers from Egypt, Pakistan and Tunisia.

In October 2020, the 67th session of the WHO Regional Committee for the Eastern Mediterranean, in resolution EM/RC67/R.2, endorsed the regional strategy to improve access to medicines and vaccines in the Eastern Mediterranean Region, 2020–2030, and urged Member States to promote local production of quality-assured medicines, including generic medicines and vaccines, to meet public health needs by developing an enabling business and regulatory environment and providing incentives.

Additionally, in October 2022, the 69th session of the Regional Committee, in resolution EM/RC69/R.2, endorsed a regional agenda for building resilient health systems towards universal health coverage and health security, which includes improving access to medicines, vaccines and health products.

To respond to the regional strategy to improve access to medicines and vaccines and the regional agenda for building resilient health systems towards universal health coverage and health security, WHO has developed this strategy in consultation with Member States and experts of the Region to ensure regional vaccine security by promoting efficient and sustainable local vaccine production.

The regional strategy focuses on four strategic objectives:

1. Establish national vaccine production policies/strategies.

Establishing national vaccine production policies/strategies in countries producing vaccines or with an active vaccine production project includes defining strategic directions and targets for vaccine production to ensure health security at country level.

2. Facilitate regional collaboration, technology transfer and partnerships.

Ensuring the sustainability of vaccine production and the security of vaccine supply in the Region, involves the development of regional collaboration between governments and establishing partnerships for health, innovation, research and development, technology transfer and vaccine supply chain.

3. Invest in research, development and production capacities.

Securing the viability and sustainability of regional vaccine production in the long-term requires investing in the development of infrastructure and the building of skills and expertise, as well as involving institutions from different sectors.

4. Strengthen regulatory capacities at national and regional levels.

Strengthening regulatory capacities and expanding the regulatory infrastructure increases the efficiency of regulatory processes and expedites the approval of vaccines. The national regulatory authority of vaccine-producing countries should attain, at a minimum, maturity level 3, as benchmarked against the WHO Global Benchmarking Tool, so that domestic vaccine producers in the Region can be eligible to apply for WHO vaccine prequalification of their products.

Introduction

Immunization is a key component of primary health care. It reduces mortality, improves life expectancy and facilitates economic growth *(1,2)*. Vaccination is one of the most powerful and cost-effective interventions in disease prevention and the control of infectious disease outbreaks *(3,4,5,6,7)*. As such, vaccines are considered one of the most cost-effective investments in health and economic development.

Equitable access to vaccines is a global priority. Ensuring quality, safety, efficacy, availability and accessibility of vaccines is critical to achieving the health Sustainable Development Goals, in particular target 3.8 on universal health coverage *(8)*. Achieving universal health coverage requires ensuring access to quality treatment for infectious diseases, investing in pandemic preparedness and strengthening health systems. However, securing the availability of high-quality vaccines at an affordable price remains a challenge for many health systems, particularly those in developing countries.

Significant progress has been achieved in the development of new vaccines against key diseases through the support of philanthropic organizations, public institutions, nongovernmental organizations and public–private partnerships. However, many infectious diseases such as Crimean–Congo hemorrhagic fever, Lassa fever, leishmaniasis, Middle East respiratory syndrome coronavirus (MERS-CoV) and Rift Valley fever are still missing a vaccine *(9)*.

The production of vaccines is enormously complex and highly regulated. The manufacturing costs are significant due to the complexity of the types of manufacturing, high risk of failure, complex logistics and stringent quality management system *(10)*.

Historically, vaccine development costs and capital investments are recovered through higher-priced sales in high-income countries. Through the initiatives of WHO and other partners, vaccines such as rotavirus vaccine and human papillomavirus vaccine have been made available to low-income countries at lower prices and in large volumes. However, these vaccines remain unaffordable, particularly for middle-income countries that are self-procuring them. Rotavirus vaccine is used in only 58% of vaccine self-procuring middle-income countries, while human papillomavirus vaccine is used in only 41% of low-income countries *(9)*.

Vaccines are medical products that are routinely administered to healthy people, and, as a result, real or perceived quality issues can compromise trust in immunization. This makes quality assurance a critical element in vaccination production *(9)*.

Over the past decades, regulatory agencies and regional networks have helped to strengthen regulatory capacities. Through its prequalification programme, WHO has been providing regulatory assistance to countries procuring through United Nations agencies. WHO has also supported countries to develop stable, well-functioning and integrated regulatory systems.

Several resolutions have been endorsed at global level by the United Nations General Assembly and World Health Assembly calling on Member States to urgently strengthen local production in order to improve equitable access to quality-assured, safe, effective and affordable medicines, vaccines and other health technologies, particularly for fighting COVID-19, by strengthening the coordination, financing, development, manufacturing, supply and distribution of the health products *(11,12,13)*. Moreover, since 1997, WHO has developed a programme to strengthen regulatory systems for vaccines to support WHO vaccine prequalification. In 2014, this programme was reinforced through the endorsement of World Health Assembly resolution WHA67.20 on regulatory system strengthening for medical products *(14)*.

In October 2020, the 67th session of the WHO Regional Committee for the Eastern Mediterranean endorsed resolution EM/RC67.2 on a regional strategy to improve access to medicines and vaccines in the Eastern Mediterranean Region, 2020–2030, including lessons from the COVID-19 pandemic *(15)*. This built on a previous Regional Committee resolution (EM/RC/51.10) endorsed in 2004 on vaccine development, accessibility and availability: towards self-sufficiency in the Eastern Mediterranean Region.

Technical paper EM/RC67/6 highlighted the need to promote research and development and the local production of vaccines and strengthen national regulatory systems. WHO was requested to support Members States to assist their national regulatory authorities (NRAs) to strengthen their regulatory systems to secure an efficient supply management system, while ensuring good manufacturing practice (GMP) requirements for local production to meet quality standards of vaccines. This stance was reiterated in 2022 in resolution EM/RC69/2 on building resilient health systems to advance universal health coverage and ensure health security in the Eastern Mediterranean Region, endorsed by Health Ministers at the 69th session of the Regional Committee *(16)*.

The development of the regional strategy to strengthen local vaccine production presented here included a regional expert consultation in June 2020, a meeting with regional ministers of health in July 2021 and a WHO regional meeting in September 2021 organized with the Coalition for Epidemic Preparedness Innovations (CEPI). These meetings identified needs and gaps regarding vaccine production in the Region and served to shape the strategy, which was presented at a pre-Regional Committee meeting in October 2022.

Situation analysis for the Eastern Mediterranean Region

The WHO Eastern Mediterranean Region has an estimated overall population of 676 million people *(17)*. In terms of gross national income levels and the development of health systems, the Region is characterized by substantial inequities and is affected by conflicts, wars and natural disasters. There is political instability in 12 of the Region's 22 countries and territories *(18)*, which presents challenges for health, and particularly for access to medicines and vaccines.

Prior to the COVID-19 pandemic

Since its introduction in 1974, the Expanded Programme on Immunization has been introduced across the Region. Vaccine demand has grown rapidly since 2000 due to population growth, an increase in national incomes and health spending, and the introduction of new vaccines to prevent diseases such as rotavirus infection, pneumonia caused by *Streptococcus pneumoniae*, and cancers caused by human papillomavirus. The modality of access to vaccines varies between the countries of the Region according to their income. Regarding access to vaccines, the countries of the Region fall into three groups based on their income level: a group of six high-income countries that have adequate access to most new vaccines with limited financial challenges; a group of eight countries that fully self-finance their vaccine procurement; and a third group of seven countries that are supported by the Gavi, the Vaccine Alliance (Gavi) *(15).* Since its creation in 2000, Gavi aims to reduce the historical delay of 15–20 years for new vaccines to reach low-income countries at an affordable price *(19)*. Gavi provides financial support for the introduction of new and underutilized vaccines (with a little co-financing) through UNICEF's Supply Division, which provides WHO prequalified life-saving vaccines for immunization programmes for a range of diseases and cash support for strengthening country health systems and improving the cold chain for immunization services *(19)*.

Most of the countries of the Region face challenges in vaccine supply, such as weak vaccine procurement and management, resulting in procurement at excessive prices, principally by non-Gavi funded middle-income countries that self-procure their vaccines *(2),* as well as high vaccine wastage, limited access to new vaccines and recurrent stock-outs.

Vaccines have been produced within the Region for over 120 years, mainly in Egypt (VACSERA), the Islamic Republic of Iran (Pasteur Institute of Iran and Razi Vaccine and Serum Research Institute) and Tunisia (Institut Pasteur de Tunis), joined later by Pakistan (National Institutes of Health).

From the 1990s, vaccine production dropped off and was even halted in Egypt, Pakistan and Tunisia for several years. Most of the vaccine producers faced problems related to a lack of quality and compliance with good manufacturing practices (GMP). In addition, these countries encountered difficulties in exporting their vaccines, as most recipient countries asked for certification of WHO prequalification of the vaccines, for which none of the regional vaccine producers were eligible. To date, most procured vaccines in the Region are imported from manufacturers headquartered elsewhere *(9)*. These vaccines are mainly WHO prequalified or manufactured in countries with NRAs recognized by WHO as functional for the regulation of vaccines.

To address GMP non-compliance and be able to apply for WHO vaccine prequalification, vaccine producers from the four regional vaccine-producing countries made substantial efforts to revamp their production facilities for traditional vaccines by building or renovating them and procuring and installing new equipment. However, this refurbishing and the resumption of effective vaccine manufacturing took many years.

In 2010, the regulatory systems of Egypt and Islamic of Republic of Iran were benchmarked against a WHO vaccine assessment tool and declared as "functional" NRAs meeting WHO and international standards.

Nevertheless, none of the regional vaccine-producing countries managed to maintain or expand their vaccine production, unlike other emerging countries that successfully manufactured vaccines meeting both WHO and international standards, and subsequently prequalifying them with WHO, such as Cuba, Brazil and India.

After the declaration of the COVID-19 pandemic

Access to vaccines was jeopardized during the COVID-19 pandemic. Lockdowns and closures negatively impacted the supply chain, slowing down local production and the supply of finished medical products *(20,21)*. This contributed to vaccine shortages and the disruption of immunization programmes, leading to concerns both regionally and globally and prompting countries in the Region to enhance vaccine production and strengthen vaccine regulation.

African countries similarly encountered difficulties in accessing medical products, including vaccines. The rollout of COVID-19 vaccines across Africa, during the pandemic, was marred by delays, scarcity and uncertainty. The African Union and the Africa Centres for Disease Control and Prevention (Africa CDC), as well as health and economic experts, called for the establishment of a continental programme to increase local vaccine production and requested support from partners for investing in vaccine manufacturing capacity to overcome health inequities. The Partnerships for African Vaccine Manufacturing (PAVM) was established under Africa CDC in 2021 and developed a framework for action in 2022 to promote continental production of 60% of the vaccines needed by 2040. Three

countries of the WHO Eastern Mediterranean Region (Egypt, Morocco and Tunisia) are African countries considered by the PAVM initiative as potential suppliers of vaccines locally manufactured in the continent.

Technology transfer agreements for COVID-19 vaccine production were made with vaccine production companies in Egypt, the Islamic Republic of Iran, Morocco, Pakistan and the United Arab Emirates. However, most of these companies imported vaccine bulks and performed "fill, finish and packaging" pharmaceutical operations, as these operations occur in the same manner regardless of the vaccine manufacturing platform.

In 2021, a global survey to assess the vaccine manufacturing capacity and capability landscape was conducted by the Coalition for Epidemic Preparedness Innovations (CEPI) *(22)*. The Eastern Mediterranean Region was included in the survey, whose respondents included government entities, veterinary institutes and manufacturers of pharmaceuticals and vaccines from three countries in Africa and four countries in the Middle East.

The survey results revealed limited or no vaccine research and development and limited capability to manufacture vaccine bulk from raw materials (drug substance). The survey also showed that only two existing vaccine manufacturers have end-to-end capability to support the production of human vaccines at medium to large scale (> 50 million doses/year) and can manufacture more than three vaccines. Aside from their differing capacities and capabilities, the focus of vaccine manufacturers is mainly on inactivated/killed, recombinant, subunit, conjugate, toxoid, or live attenuated vaccine production and there is a lack of experience in the Region in DNA/mRNA and lipid nanoparticle vaccine technologies.

Following requests from vaccine-producing countries in the Region to strengthen their vaccine regulatory system, WHO worked to assess their respective regulatory authorities using the WHO Global Benchmarking Tool (GBT) that was issued in 2018. In 2022, the results of the assessment of Egypt's NRA showed it to be well functioning and reliable, with an integrated and stable regulatory system, and accordingly, had reached maturity level 3. Maturity level 3 of the NRA is a prerequisite for eligibility for the WHO vaccine prequalification assessment, so this allows Egyptian vaccine manufacturers to apply for WHO prequalification for their domestic vaccines. The Iranian NRA has been considered as functional by WHO since 2010 and a re-evaluation using the current WHO GBT is planned. In addition, the NRAs of Morocco, Pakistan, Saudi Arabia, Tunisia and the United Arab Emirates have initiated the benchmarking process and will be evaluated over the next couple of years.

Challenges

Vaccine production is complex and hard to sustain. The most important aspect is the need to ensure safety, efficacy, quality and consistency over the life cycle of a vaccine. The various steps in the upstream processing, downstream processing and formulation of biologic-derived vaccines have notable differences depending on the manufacturing method *(23)*. The complexities of vaccine production also include the biological variability in the starting materials, the environmental condition of the microbial culture, the knowledge and experience of the manufacturing technician and the steps involved in the purification process, as well as the inherent variability of the quality control methods used *(24)*.

For over 20 years, vaccine-producing countries in the Region have faced numerous challenges, largely due to the lack of a coherent vision or strategic plan at the national level, resulting in insufficient support for local vaccine producers, and also to the absence of a common regional plan and demand forecasting for coordinated planning, financing and activities. For instance, several

countries in the Region have invested in COVID-19 vaccine manufacturing facilities without consulting or informing each other. Coordination and consultation among countries is important for achieving economies of scale, and hence sustainability.

One of the most important challenges is the lack of full GMP compliance by vaccine manufacturers in the Region. Inappropriate facilities and equipment, inadequate quality control, inappropriate documentation and a failure to follow standard operating procedures for product recalls were all reported during WHO assessments of the Region's vaccine regulatory systems.

Another key challenge is ensuring the biomanufacturing workforce has the necessary knowledge and skills. Moreover, when competent and experienced staff are in place, it can be difficult to retain them as they are not appropriately paid or incentives to retain and motivate them do not exist.

Ensuring the supply of raw materials, reagents, biological reference materials, cell lines, vaccine seed strains, materials and equipment such as ultracentrifuges, bioreactors and vaccine vial monitors, presents another challenge for vaccine manufacturing for a number of reasons. These include high prices, the limited number of qualified suppliers and difficulties in production *(24)*. A lack of access to raw materials such as excipients, glass vials, rubber stoppers and fermentation bags was witnessed during the peak period of the COVID-19 pandemic, when supply chain problems, including the disruption of transportation, presented a critical obstacle for national and regional responses *(20,21)*.

The regulatory systems of most of the vaccine-producing countries in the Region need to be strengthened to meet WHO regulatory requirements and ensure the functionality (i.e. attaining maturity level 3 at a minimum) of the NRA for market authorization and registration, licensing of manufacturers, regulatory GMP inspection, vaccine lot testing and release, regulatory oversight of clinical trials and evaluation of clinical performance, market control, and surveillance of, and vigilance over, locally-manufactured vaccines to ensure their quality, safety and efficacy. Key challenges for regulation in the Region include the lack of legal and regulatory frameworks, lack of skills and expertise in the regulation of vaccines, non-existent or weak quality management systems encompassing all regulatory functions, an absence of documentation systems such as guidelines, procedures and records, and a lack of evidence.

Although there are research institutions in several countries, there is limited research and development in vaccine production technology within the Region, except in the Islamic Republic of Iran which was able to develop more than nine COVID-19 vaccines *(5)*.

Considerations for successful and sustainable vaccine production

There are some key considerations that should be taken into account to ensure successful and sustainable local vaccine production in the long term.

Key components need to be in place, including: strong government support; sufficient financial resources; adequate infrastructure and vaccine manufacturing capacity; a well-functioning and stable regulatory system; skilled human resources and continuous and appropriate workforce development and capacity-building; partnerships and scientific/technology transfer; a secured supply chain for raw materials, reagents and equipment; research and development capacity; and good knowledge of the vaccine market and country demand for vaccines *(10,25,26)*.

Every country needs to establish its own national vaccine policy/plan to ensure access to vaccines, within its national health strategic plan, with the aim of ensuring national vaccine equity and security.

Local vaccine production should be seen as a national health security objective and part of a resilient health system. There needs to be long-term political commitment to encouraging manufacturers to produce vaccines. Vaccine-producing countries should have a clear country-specific vaccine production or industrial policy that defines how and when to consider local vaccine production, supports vaccine manufactures in defining priorities and in the selection of the types of vaccine and technology platforms for production to meet national public health needs, and facilitates the export of the vaccines *(27)*. Governments, with the involvement of the vaccine manufacturers, should develop a national policy and a strategy for vaccine production.

Key elements in strengthening vaccine production include promoting innovation and research and development, strengthening infrastructure, securing sufficient financial resources, including financial incentives (such as tax flexibility), strengthening governance arrangements and regulatory infrastructure.

Government investment is needed during the initial stages to foster local vaccine production, establish and maintain a strong regulatory system, support workforce development, facilitate a conducive business environment and encourage the use of local products in the local market. This is a key factor in achieving successful and sustainable local vaccine production *(28)*.

Technology transfer provides an effective strategy for accelerating production capacity and can contribute significantly to increasing vaccine supply and facilitating access to vaccines and reducing their price. This has been well demonstrated by technology transfer of the *Heamophilus influenzae* type b, hepatitis B and meningitis A vaccines *(29)*. However, technology transfer opportunities are limited because finding companies willing to share their technical knowledge and invest resources in transferring their knowledge or products to another company can be a challenge since the recipient companies can be perceived as potential future competitors *(29)*. WHO can play an important role in facilitating technology transfer when needed.

Successful technology transfer to the recipient production sites relies on several key factors. These include the facility's compliance with GMP requirements, investment in specific equipment and skilled personnel, and an NRA that can effectively regulate vaccines.

Expanding vaccine manufacturing without adequate regulatory capacity can lead to poor product quality, potentially resulting in adverse effects that undermine public trust and compromising prequalification and export.

An effective and harmonized regulatory process within the Region to facilitate the regulation and control of vaccines will contribute to the sustainability of vaccine production at national and regional levels.

A feasibility study to evaluate the key components needed for successful and sustainable local vaccine production is required to assist countries deciding on investing in vaccine production.

Nevertheless, given that vaccine manufacturing is one of the most challenging industries and the vaccine market is limited compared to the medicines market, not all countries will find it feasible to invest in vaccine production.

However, countries in the Region should consider investing in the production of raw materials, excipients and consumables or in the provision of clinical research services through contract research organizations (CROs), including organizing and managing pre-clinical and clinical trial studies, bioanalytical testing, statistical analysis, assembling regulatory dossiers for clinical trial applications,

and pharmacovigilance. Most countries of the Region can therefore contribute directly or indirectly to regional vaccine production.

Countries should also consider participating in regional collaboration and agreeing on a division of responsibilities, whereby certain countries invest in manufacturing the ingredients, accessories and materials needed for the vaccine production cycle or in providing clinical research or pharmacovigilance services. The regional strategy will support the strengthening of collaboration and partnerships among the countries of the Region.

Aim

The aim of the regional strategy is to ensure regional vaccine equity and security by promoting efficient and sustainable vaccine production at the regional level to support the elimination and control of vaccine-preventable diseases and preparation for a rapid response to outbreaks and epidemics, including of emerging infectious diseases.

Objectives

The regional strategy is built around four strategic objectives:

Strategic objective 1. Establish national vaccine production policies/strategies

While a national vaccine policy or strategic plan for ensuring access to vaccines should be developed in all countries of the Region, a national vaccine production policy/strategy should be developed by any country that is producing vaccines or has an active vaccine production project. This should define strategic directions and targets for vaccine production that will ensure health security at national level. Defining the strategic directions and targets should involve all relevant stakeholders from the health, research and economic sectors, and will entail identifying the public health needs and development objectives as well as aligning the vaccine production policy/strategy with any overall national health vision and policy.

Key actions

The following are the key actions for the different stakeholders that contribute to the strengthening of national vaccine production governance.

All countries of the Region:

- Elaborate a vaccine policy/strategic plan to ensure access to vaccines in a timely manner.

Vaccine-producing countries:

- Conduct a "mapping exercise" at national level to identify the key national stakeholders to ensure all relevant stakeholders are engaged and their capacities leveraged.
- Ensure long-term political commitment.
- Secure financial resources and investment from government.
- Implement a national vaccine production strategic plan, covering research and development, regulation and the procurement of vaccines.
- Develop an economic model (using feasibility studies and business models) for vaccine production.

Non-vaccine producing countries:

- Explore the feasibility of producing the raw materials, ingredients and accessories that are needed for vaccines and other medical products, and/or developing CRO activities/services related to vaccines.

WHO:

- Provide technical support for developing and implementing national vaccine production and research policies.
- Conduct a vaccine production ecosystem assessment in the Region.
- Conduct a gap analysis for GMP in vaccine production facilities in the Region.
- Conduct, in close collaboration with governments and other parties, regional mapping of needs and requests for vaccine manufacturing.

Other development partners:

- Provide technical support for conducting feasibility studies and the development of vaccine production business models.
- Provide financial support for conducting feasibility studies and developing vaccine production business plans.
- Provide financial support for the regional mapping of needs and requests for vaccine manufacturing.
- Provide financial support for investment in the production of the key ingredients/consumables needed for vaccine production.

Vaccine manufacturers

- Develop a strategic plan to implement the national strategic plan.
- Establish economic models, including through feasibility studies and business plans.

Strategic objective 2. Facilitate regional collaboration, technology transfer and partnerships

Strengthening collaboration and partnerships for health, innovation, and research and development between country governments is key to ensuring the sustainability of regional vaccine production. Hence, it is important to establish regional networks for research and development and the production of vaccines, and to reach agreements at the regional level on logistics, procurement of vaccines and manufacture of raw materials.

Public-private partnerships between public institutions, academia and private organizations at national level can contribute to strengthening vaccine production and accelerate research and development through the private sector's more flexible governance and funding mechanisms, and more efficient management of funds. This will contribute to long-term sustainability.

International partnerships, including for technology transfer, should be supported and facilitated by recipient governments to ensure financial investment. This includes the potential involvement of key partners, such as international nongovernmental organizations, in supporting production capabilities through addressing financial and trade barriers and facilitating the export of vaccines.

International collaboration with international organizations such as WHO, United Nations Industrial Development Organization (UNIDO) and international financial institutions is essential for facilitating collaboration at the regional level and supporting technical cooperation and information-sharing among countries.

Implementing regional harmonization of regulatory standards would lead to improved regional health security by enabling established regional manufacturers to supply vaccines throughout the Region. This would increase the timely access to vaccines, reduce the costs and time taken to obtain regulatory approval in countries and contribute to the incentivization of vaccine producers.

Key actions

The following are the key actions for the different stakeholders that contribute to strengthening regional collaboration and partnerships.

All countries:

- Identify vaccine manufacturers in the region including those with active development project
- Agree on the types of vaccines needed for the Region based on the regional epidemiological situation and public health needs.
- Engage in coordination and collaboration to support vaccine production in selected countries.

Vaccine-producing countries:

- Select a technology transfer model appropriate to the country's capacity and specificities.
- Acquire technology and knowledge transfer.
- Establish appropriate agreements with the technology transfer donor to ensure successful and comprehensive technology transfer.
- Establish a regional network for vaccine production.

Non-vaccine producing countries:

- Support implementation of the production of some key ingredients/consumables needed for vaccine production.

WHO:

- Facilitate the development of regional vaccine manufacturing collaborative partnerships to coordinate and deliver vaccine manufacturing capacity/capability programmes.
- Coordinate and collaborate with national health authorities to promote technology transfer and interregional activities for innovation and research and development.
- Provide local manufacturers with appropriate information on the selection of technology transfer models and development of agreements to ensure acquisition of the full technology (the full production process).
- Promote the establishment of a regional network/platform among vaccine manufacturers to share experiences and information among countries and build capacity.
- Promote regional harmonization and convergence of vaccine regulation to ensure timely regulatory approval of vaccines.
- Promote regional collaboration and the establishment of a regional network of NRAs.

Other development partners:

- Facilitate the development of regional vaccine manufacturing collaborative partnerships to coordinate and deliver vaccine manufacturing capacity/capability programmes.
- Provide financial support for conducting feasibility studies and developing vaccine production business plans.
- Support technology and knowledge transfer.

Vaccine manufacturers:

- Establish a regional network among vaccine manufacturers in the Region to share experience and build capacity.
- Establish technology transfer agreements based on the selected vaccines.

Strategic objective 3. Invest in research, development and production capacities.

Ensuring the viability and sustainability of vaccine production in the long-term requires investment in the development of infrastructure, skills and expertise, as well as the involvement of institutions from different sectors. There is a need for strong research and development capacity, the ability to produce raw biological ingredients and other materials, and the availability of CRO services.

Key actions

The following are the key actions for different stakeholders that contribute to strengthening research and development and production capacities.

Vaccine-producing countries:

- Identify funding opportunities/grants to support research and development for vaccine production.
- Invest in capacity-building to ensure implementation of standard practices (GxP) in vaccine regulation, manufacturing, clinical development, laboratory practices, storage and distribution, and quality management.

WHO:

- Establish regional training centres to facilitate support for training in areas related to vaccine development and production, including GMP, quality control and quality assurance, non-clinical and clinical vaccine development, good clinical practices, development of chemistry, manufacturing and controls (CMC) procedures and common technical documents (CTDs), laboratory testing, ethics, vigilance and scientific writing.
- Support the improvement of vaccine production facilities in countries.
- Facilitate support for training and capacity-building in vaccine research and development, production processes and quality management.
- Assist manufacturers to achieve compliance with WHO prequalification or EUL.

Other development partners:

- Provide financial support to strengthen research and development and production capacities.

Vaccine manufacturers:

- Invest in a capacity-building plan to ensure implementation of GxP and meet quality system requirements.
- Develop a corporate plan to achieve GMP and implement a quality management system towards submission of vaccines for WHO prequalification or WHO EUL in case of pandemics and consideration for potential pooled regional vaccine procurement.
- Build capacity and develop workforce skills in vaccine production processes.

Strategic objective 4. Strengthen regulatory capacities

Strengthening the vaccine regulatory system of vaccine-producing countries and countries engaged in vaccine development and research is vital. Indeed, regulation is essential for the entire vaccine value chain, and is involved in nearly every aspect of vaccine development, manufacturing and marketing approval. Regulations come into play from the time of vaccine design and clinical testing, through the manufacturing process, to when the final product is distributed for widespread use. Strengthening regulatory capacities and expanding regulatory infrastructure increases the efficiency of regulatory processes and expedites the approval of vaccines.

The NRA's role is critical for manufacturers to be able to commercialize and market their domestic products within a country and/or export them throughout the Region or around the world. The NRA of vaccine-producing countries should attain, at a minimum, maturity level 3 of the WHO GBT so that vaccine producers can become eligible to apply for WHO vaccine prequalification of their products.

Key actions

The following are the key actions for different stakeholders that contribute to strengthening regulatory capacities at national and regional levels.

All countries:

- Develop or enact appropriate legal provisions and regulations.
- Establish good governance, including policies.
- Ensure adequate infrastructure and facilities, with adequate and sufficient equipment and materials.
- Ensure regulatory process and mechanisms are in place to ensure the quality, safety and efficacy of supplied vaccines.
- Implement quality management systems for all regulatory functions.
- Invest in the capacity-building of regulators to increase their skills.
- Develop an institutional development plan and roadmap to strengthen the vaccine regulatory system for achieving, at a minimum, maturity level 3.

Vaccine-producing countries:

- Implement stringent quality standards to obtain WHO prequalification for vaccines manufactured in the country.

WHO:

- Provide support to countries for strengthening their NRA to reach, at a minimum, maturity level 3, prioritizing vaccine-producing countries and countries providing vaccine development services.
- Provide capacity-building to countries to strengthen regulatory capacities.
- Provide technical support to countries to strengthen regulatory capacities.
- Facilitate placements of NRA staff in other regulatory agencies that have maturity level 3 or 4 or are a WHO-Listed Authority (WLA).

Other development partners:

- Provide financial support for capacity-building and regional networking.

Vaccine manufacturers:

- Improve quality management and quality assurance systems.
- Implement current GMP.
- Build capacity and develop workforce skills in vaccine regulation.

Implementing the strategy

Annex 1 illustrates the roles and responsibilities of the key stakeholders at country level, including WHO, national governments and vaccine manufacturers, and the contribution of partners, in implementing the regional strategy to strengthen local vaccine production.

Monitoring and evaluation of the strategy

Annex 2 outlines a monitoring and evaluation framework, including a set of indicators and targets for each of the strategic objectives, to monitor progress on the implementation of the regional strategy.

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Annex 1. Roles and responsibilities of key stakeholders in implementing the regional strategy to strengthen local vaccine production

The engagement and support of key stakeholders is needed to implement the regional strategy to strengthen local vaccine production. These stakeholders include the countries and territories of the Eastern Mediterranean Region, supported by WHO, vaccine manufacturers and development partners. The success of the plan depends on collective ownership and shared accountability. The table below outlines the roles and responsibilities of the various stakeholders.

Strategic objective	**National governments**			**WHO**	**Other development partners**	**Vaccine manufacturers**
	All countries of the Region	**Vaccine-producing countries**	**Non-vaccine producing countries**			
Establish a national vaccine production policy/ strategy	• Elaborate a vaccine policy/strategic plan to ensure access to vaccines in a timely manner.	• Conduct a "mapping exercise" at national level to identify the key national stakeholders, to ensure all the relevant stakeholders are engaged and their capacities leveraged. • Ensure long-term political commitment. • Secure financial resources and investment from government. • Implement a national vaccine production strategic plan, including for research and development, regulation and the procurement of vaccines, and develop a roadmap to monitor implementation. • Establish economic models (using feasibility study and business models) for vaccine production.	• Explore the feasibility of producing the raw materials, ingredients and accessories that are needed for vaccines and other medical products and/or developing CRO activities/services related to vaccines.	• Provide technical support for developing and implementing national vaccine production and research policies. • Conduct a vaccine production ecosystem assessment in the Region. • Conduct a gap analysis for GMP in vaccine production facilities in the Region. • Conduct, in close collaboration with governments and other parties, regional mapping of needs and requests for vaccine manufacturing.	• Provide technical support for conducting feasibility studies and the development of vaccine production business models. • Provide financial support for conducting feasibility studies and developing vaccine production business plans. • Provide financial for the regional mapping of needs and requests for vaccine manufacturing. • Provide financial support for investment in the production of the key ingredients/consumables needed for vaccine production.	• Develop a strategic plan to implement the national strategic plan. • Establish economic models (feasibility study/establishing business models).

Strategic objective	National governments			WHO	Other development partners	Vaccine manufacturers
	All countries of the Region	Vaccine-producing countries	Non-vaccine producing countries			
Facilitate regional collaboration, technology transfer and partnerships	• Identify vaccine manufacturers in the region including those with active development project. • Agree on the types of vaccines needed for the Region based on the regional epidemiological situation and public health needs. • Engage in regional coordination and collaboration to support vaccine production in selected countries.	• Select a technology transfer model appropriate to country capacity and specificities. • Acquire technology and knowhow/knowledge transfers. • Establish appropriate agreements with the technology transfer donor to ensure successful and comprehensive technology transfer. • Establish a regional network for vaccine production.	• Support implementation of the production of some key ingredients/consumables needed for vaccine production	• Facilitate the development of regional vaccine manufacturing collaborative partnerships to coordinate and deliver vaccine manufacturing capacity/ capability programmes. • Coordinate and collaborate with national health authorities to promote technology transfer and interregional activities for innovation and research and development. • Provide local manufacturers with appropriate information on the selection of technology transfer models and development of agreements to ensure acquisition of the full technology (the full production process). • Promote the establishment of a regional network/platform among vaccine manufacturers to share experience, information among Member States and build capacity. • Promote regional harmonization and convergence of vaccine regulation to ensure timely regulatory approval of vaccines. • Promote regional collaboration and the establishment of a regional network of NRAs.	• Facilitate the development of regional vaccine manufacturing collaborative partnerships to coordinate and deliver vaccine manufacturing capacity/capability programmes. • Provide financial support for conducting feasibility studies and developing vaccine production business plans. • Support technology and knowledge transfer.	• Establish a regional network among vaccine manufacturers in the Region to share experience and build capacity. • Establish technology transfer agreements based on the selected vaccines.

Strategic objective	National governments			WHO	Other development partners	Vaccine manufacturers
	All countries of the Region	Vaccine-producing countries	Non-vaccine producing countries			
Invest in research, development and production capacities		• Explore funding opportunities/grants to support R&D for vaccine production. • Invest in a capacity-building plan adapted to ensure implementation of GxP (good practices for regulation, manufacturing, clinical, laboratory, storage, distribution, etc.) and quality system requirements. • Develop a corporate plan to achieve GMP and implement a quality management system towards submission of the vaccine for WHO prequalification or WHO EUL in case of a pandemic and being considered for potential supply at regional or global levels.		• Establish regional training centres to facilitate support for training in areas related to vaccine development and production, including GMP, quality control and quality assurance, non-clinical and clinical vaccine development, good clinical practices, development of CMC procedures and CTDs, laboratory testing, ethics, vigilance and scientific writing. • Support the improvement of vaccine facilities in countries. • Facilitate support for training and capacity-building in vaccine research and development, production processed and quality control management. • Assist manufacturers to achieve compliance with WHO prequalification or EUL.	• Provide financial support to strengthen research and development and production capacities.	• Invest in a capacity-building plan to ensure implementation of GxP and meet quality system requirements. • Develop a corporate plan to achieve GMP and implement a quality management system towards submission of vaccines for WHO prequalification or WHO EUL in case of pandemics and consideration for potential pooled regional vaccine procurement. • Build capacity and develop workforce skills in vaccine production processes.

Strategic objective	National governments			WHO	Other development partners	Vaccine manufacturers
	All countries of the Region	Vaccine-producing countries	Non-vaccine producing countries			
Strengthen regulatory capacities	• Develop or enact appropriate legal provisions and regulations. • Establish good governance, including policies. • Ensure adequate infrastructure and facilities, with adequate and sufficient equipment and materials. • Ensure regulatory process and mechanisms are in place to ensure quality, safety and efficacy of supplied vaccines. • Implement quality management systems for all regulatory functions. • Invest in capacity-building of regulators to increase their skills. • Develop an institutional development plan and roadmap to strengthen the vaccine regulatory system for achieving, at a minimum, maturity level 3.	• Country governments should provide support to enable the NRAs to implement stringent quality standards for getting WHO prequalification of the vaccines manufactured in the Region, then reaching at minimum maturity level 3.	• Implement stringent quality standards to obtain WHO prequalification for vaccines manufactured in the in the country.	• Provide support to countries for strengthening their NRA to reach, at a minimum, maturity level 3, prioritizing vaccine-producing countries and countries providing vaccine development services. • Provide capacity-building to countries to strengthen regulatory capacities. • Provide technical support to countries to strengthen regulatory capacities. • Facilitate placements of NRA staff in other regulatory agencies that have maturity level 3 or 4 or are a WHO-Listed Authority (WLA).	• Provide financial support for capacity-building and regional networking.	• Improve quality management and quality assurance systems. • Implement current GMP. • Build capacity and develop workforce skills in vaccine regulation.

Annex 2. Monitoring and evaluation framework

The monitoring and evaluation framework outlined below consists of a set of indicators for each of the strategic objectives to be used to monitor progress on the implementation of the regional strategy.

Strategic objectives	**Indicator**	**Target 2023**	**Target 2033**
Establish a national vaccine production policies/strategies	Number of vaccine-producing countries with a national industrial policy	0	4
Facilitate regional collaboration, technology transfer and partnerships	Regional network for vaccine manufacturers established	0	1
Invest in research, development and production capacities	Number of WHO prequalified vaccines	0	2
Strengthen regulatory capacities	Number of NRAs of vaccine-producing countries with, at a minimum, maturity level 3	1	4
	Number of NRAs designated as a WLA	0	2
	Regional network for vaccine regulation established	0	1