SP6

SUPPLY SECURITY

Introduction and value proposition

Immunization programmes require secure access to vaccines in order to achieve public health goals. Vaccine supplies are secure when all communities everywhere have timely and reliable access to vaccines that are safe, efficacious, quality-assured, affordable and programmatically suitable for the settings where they will be used. To achieve vaccine supply security, all countries need an understanding of vaccine market dynamics, regulatory capacity and the ability to efficiently procure vaccines, while global production needs to be sufficient to meet the current and projected aggregated needs of countries.*

Unfortunately, both high- and low-income countries sometimes struggle to secure timely supplies of appropriate vaccines. Barriers include high prices, insufficient funding, planning challenges, supply shortages, lack of suitable or preferred products and surges in demand that exceed available supplies. Supply insecurity can occur when there is inadequate flow of funding at the time of procurement, poor planning capacity, or lack of appropriately trained staff. Supply insecurity can also result from regulatory issues at the manufacturer, global or country level, poor access to the information needed for decision making, and the challenges inherent in complex biological products. Commercial interests and national policies that affect the private sector can also have a major impact. Supply challenges are amplified in the time-sensitive and often politically charged contexts of humanitarian emergencies as well as regional outbreaks and pandemics such as Ebola and COVID-19.

Addressing these needs will require **healthy *global* vaccine markets** that serve all stakeholders, as well as political commitment and enhanced procurement and regulatory processes that support vaccine availability and affordability.[2] A healthy market is appropriately regulated, responsive to country needs, incentivizes manufacturers and suppliers, and rewards innovation. It meets the needs of both manufacturers and consumers, with sustainable prices that are affordable over the long term. It ensures a reliable supply of high-quality, affordable vaccines for routine use as well as in emergencies and pandemics.

---

* Note. This annex focuses on supply security from an access perspective. See SP1, UHC/PHC for a discussion of country-level supply chain strengthening.

Various "healthy market frameworks" have been developed that document demand and supply dynamics, diagnose root causes, and inform strategies to improve market health.[1] IA2030 calls on stakeholders to apply the healthy markets approach globally to all vaccines and countries, including vaccines for emerging infectious diseases, and to work together to improve vaccine supply security for everyone.

Strategic Priority Goal and Objectives

Goal

All countries have a reliable supply of appropriate and affordable vaccines of assured quality and sustainable financing for immunization programmes

Objectives

1. Build and maintain healthy global markets across all vaccine antigens
2. Ensure sufficient financial resources for immunization programmes in all countries
3. Increase immunization expenditure from domestic resources in aid-dependent countries and, when transitioning away from aid, secure government funding to achieve and sustain high coverage for all vaccines

This annex addresses objective 1. See the SP6 Sustainable Financing for Immunization annex for a discussion of objectives 2 and 3.

Context and challenges

The global vaccine marketplace is complex, due to the diversity of vaccine buyers, products and manufacturers.

Buyers. Governments are often the primary buyers of vaccines. They can be grouped on the basis of capacity and access to financial support.

- **Countries that are eligible for Gavi support** can access support for vaccine purchases and health systems improvements. They may experience vaccine shortages or stockouts due to regulatory issues, inaccurate forecasting and poor stock management, or when domestic resources are not available when needed (see SP6 Sustainable Financing annex). They may also have product preferences that markets cannot meet on a timely basis. Decisions by manufacturers to prioritize certain markets over others also contribute to inadequate supply and stockouts.
- **Lower capacity countries** include non-Gavi countries that receive little external support and have fewer resources and less procurement capacity than higher capacity countries. Lower capacity countries can experience difficulties in securing vaccines for multiple reasons, including: high prices and insufficient supply availability, especially for new vaccines; insufficient decision-making capacity; urgent competing needs and stressors such as economic downturns and civil strife that affect funding; and weaknesses in planning, forecasting and procurement.[2,3] Challenges are particularly acute for countries that are transitioning away from donor aid.

- **Higher capacity countries** are often attractive markets and tend to be prioritized by manufacturers for supply allocation. They often include private markets, where there may be a willingness to pay higher prices. Higher capacity countries can experience vaccine stockouts due to procurement delays and global vaccine shortages.[4]

Other important buyers influence markets and require secure access to vaccines. These include: private sector healthcare providers; pooled procurement mechanisms such as those managed by UNICEF, the Pan-American Health Organization (PAHO), and the Gulf Cooperation Council; humanitarian agencies such as Doctors Without Borders and the UN High Commission for Refugees; non-governmental organizations; and global stockpiles for outbreak and epidemic response.

Products. Vaccine supply dynamics are complex for multiple reasons. First, vaccines are used in a variety of target populations. Some have global markets while others are recommended for routine vaccination only in certain regions or for specific populations at higher risk.[5] Secondly, vaccine markets include both "traditional" vaccines that have been in use for many years and "innovator" vaccines. Innovator vaccines are typically produced by a limited number of manufacturers, leading to access challenges and supply security risks. Manufacturers may also expect higher returns due to uncertain demand or to recoup investments in research and development.[6] Finally, vaccines for the same disease are not necessarily interchangeable due to differences in composition, vaccination schedule, packaging and presentation, or due to regulatory and legislative requirements that limit the product choices available to a country.[4]

Manufacturers. Supply sustainability requires a healthy ecosystem, including healthy industry. Vaccine manufacturers include multinational corporations, developing country vaccine manufacturers (DCVMs) and state-owned entities. Multinational corporations are often product innovators. They typically charge higher prices to high-income countries and lower prices for greater volumes in low- and middle-income countries. DCVMs have helped to increase product choices and global manufacturing capacity, contributing to supply security and bringing competition that can lower prices. Because of their high-volume, low-cost business models, DCVMs account for 65% of vaccine doses manufactured globally but a much smaller share of global vaccine revenues.[6]

Key Areas of Focus

To improve vaccine supply security, IA2030 defines four interrelated key focus areas where action is required to improve market health. The interventions described below must be refined, expanded and operationalized over this decade by all stakeholders, from industry to communities, to ensure sustainable healthy markets that serve everyone.

This is especially true as the world is grappling with COVID-19. This pandemic has led to unprecedented collaboration to ensure affordability and access to COVID-19 vaccines, sparking innovations as well as the scaling of proven ap-

proaches such as advance market commitments. It has heightened the awareness of health inequities and raised our ambitions for tackling them. These focus areas must play a role in the COVID-19 response and in turn will be updated to capture the lessons and opportunities that emerge from the response.

Innovation and affordability

Ensure that the supply of and access to new vaccines meet country needs and that vaccines are introduced in a timely manner, regardless of a country's wealth, and at a price that is affordable.

Key evidence and gaps

New products developed for higher capacity countries may not be designed for or tested in populations in other settings. They may not be appropriate, programmatically suitable, or available in a timely manner and at affordable prices for lower capacity countries.[7]

Market-shaping interventions over recent decades have helped to accelerate access, reduce vaccine prices and incentivize innovation to meet the needs of countries, especially those procuring through the PAHO Revolving Fund and through UNICEF. Strategic and financial intervention by Gavi, the Vaccine Alliance has also improved access for eligible lower- and lower middle-income countries and contributed to significant reductions in vaccine prices for eligible countries.[1] Market-shaping interventions have included:

- **Product development investments** that have brought new vaccines and additional suppliers to the market, adding to total supply and increasing price competition. Because many of these suppliers are DCVMs, these investments have also helped to build regional manufacturing capacity, especially in South Asia.
- **Advance market commitments, advance purchase commitments and volume guarantees,** which have lowered risks for manufacturers and incentivized product development and capacity building for low-income markets.[8]
- **Improved demand forecasting,** which has reduced risks and increased confidence by allowing manufacturers, countries and funders to align their strategies. It has helped manufacturers judge production needs and improve efficiency, thereby lowering costs and reducing risk.
- **Pooled procurement,** which has consolidated demand and reduced transaction costs.[4]
- **Vaccine stockpiles and the "humanitarian mechanism",** which have improved access to vaccines in outbreaks and emergencies, as discussed in Section 4.4.

Many unmet needs remain, especially for lower-capacity countries not eligible for Gavi support. These countries have experienced delays in introducing new vaccines, due in part to prices higher than can be funded with available resources.[3] Suppliers face challenges such as demand shifts as countries transition out of Gavi eligibility, difficulties in predicting product

preferences, long-term agreements for which demand does not fully materialize, and markets moving quickly from undersupply to oversupply due to similar pipelines. To address these needs, IA2030 aims to build and maintain healthy markets for vaccines.

Strategic interventions

To meet public health goals, market improvement strategies should be prioritized for all vaccines and vaccine delivery devices. As the basis for these strategies, WHO, UNICEF, PAHO, Gavi and other partners should develop **global vaccine market assessments that identify potential approaches to achieve and sustain healthy global markets.** These assessments should:

- Be developed in partnership with stakeholders, including industry.
- Build on the WHO Market Information for Access programme, UNICEF Market Notes, Gavi market roadmaps, analysis from the PAHO Revolving Fund, market information from regional access schemes such as in the EU, and data from large countries.[9,10]
- Be informed by research into market dynamics and procurement, including research on the factors that influence country decisions and vaccine uptake and on ways to improve affordability while still providing incentives for industry.
- Identify important policy changes, such as new or revised recommendations from WHO.
- Identify important pipeline changes, including new products, formulations, or presentations and improvements in existing products.
- Consider the operational and programmatic factors that shape short-term dynamics such as cold chain requirements, product presentation and product interchangeability.
- Consider short-term demand–supply balance and recognize the interdependencies among different market segments.
- Generate demand forecasts.
- Highlight affordability issues and supply availability constraints, particularly for most desired vaccine formulations and presentations.
- Identify opportunities for innovation and track progress over time to inform future market-shaping strategies.

Through a global dialogue driven by country needs, these market assessments should become the basis for **shared strategies to improve market health,** especially for lower capacity countries. Strategies may include product development investments, technology transfer, building capacity for vaccine production, or shifting to modular manufacturing to increase flexibility in how capacity is used. They may include advance market commitments and tendering strategies designed to achieve aims such as supplier diversity or availability of products meeting specified target product profiles. As shown by the synchronized

global switch from trivalent to bivalent oral poliovirus vaccines, deliberate strategies that clearly define how stakeholders will collaborate can achieve ambitious goals.[11] These market assessments will inform how countries, regulators, manufacturers, procurement entities and policymakers engage and collaborate, with the ultimate aim of ensuring sustainable and accessible supplies of quality vaccines.

Assumptions and risks: Accurate market assessments will require information sharing among countries, manufacturers and procuring entities. Since pricing and supply information can be confidential and sensitive, stakeholders, including countries and manufacturers, need to understand the value of improved market transparency and will require appropriate and trustworthy mechanisms for data collection and synthesis in order to fully participate in this system.

Market-shaping interventions require resources. As such, there is a risk that inequities in investment will perpetuate inequities in access. Well-informed market assessments can mitigate this risk by enabling pragmatic approaches that improve access to the degree possible with available resources and by motivating increased investment. In addition, cooperative mechanisms to promote equitable distribution of vaccines, such as the COVAX Facility, have been launched in response to the COVID-19 pandemic. The lessons learned from these mechanisms will inform market-shaping strategies for other vaccines.

Vaccine forecasting, procurement and supply

Improve national and global forecasting, planning and procurement capability to safeguard affordable, sustainable supplies and strengthen relations with manufacturers to ensure that vaccine production and supply meet national needs in all countries.

Key evidence and gaps

Current vaccine markets are not efficiently serving the needs of all consumers due in part to gaps and challenges in vaccine planning, forecasting, procurement and supply.

Manufacturers rely on demand forecasts to set priorities and plan production. Credible demand forecasts enable appropriately scaled production, lower costs and more stable supply.[12] Manufacturers have limited ability to respond when forecasts are inaccurate, due to long lead times for manufacturing, ranging from several months to three years, the limited availability of certain raw materials, and the need to maximize utilization of production capacity. Without reliable forecasts, manufacturers risk losses due to unused capacity, while immunization programmes risk stockouts and unmet needs, or over-stocking and wastage. Consistently inaccurate forecasts can also cause suppliers to exit from the market.

Demand forecasts are sometimes unreliable. As discussed in SP6 Sustainable Financing, some countries do not have clear strategic planning processes, leading to disconnects in decision making and planning. For example, some policymakers wait until prices are set and supply is available before making decisions, while others make major programmatic decisions such as scheduling vaccination campaigns without considering whether supplies are adequate. These disconnects

contribute to inaccurate forecasts of vaccine demand. In addition, many countries focus on short-term or annual immunization policies, forecasting, budgeting and procurement. This can lead to sudden changes in demand for specific products that increase the risk of shortages.

Some countries lack efficient procurement systems. Sixty percent of all vaccine doses are self-procured by countries, with middle-income countries procuring 91% of those doses. Depending on the procurement approach used, self-procured vaccines may be more expensive than vaccines purchased through pooled procurement mechanisms such as those managed by UNICEF and PAHO.[4,6] Self-procuring countries, including countries that have state-owned manufacturing facilities, need efficient procurement systems to keep pace with changes in the vaccine market. These needs can be met by improving procurement capacity and access to market intelligence, or by removing the programmatic, administrative and legal barriers to the use of pooled procurement mechanisms.

Pooled procurement mechanisms consolidate demand, increase bargaining power, stabilize supply and lower costs through approaches such as long-term contracts and sourcing through multiple suppliers. UNICEF and PAHO's pooled procurement mechanisms work with UNICEF's Vaccine Independence Initiative and the PAHO Revolving Fund, which give countries access to sustainable lines of credit, ensuring that countries have continuous and reliable vaccine supplies and that suppliers have sustained demand and prompt payment. Additional pooled procurement mechanisms exist or are being developed to serve the needs of other regions and country groups. Some countries are unable to use pooled procurement mechanisms due to operationalization or investment challenges, or regulatory or legal barriers.[13] Cross-country collaborations to improve vaccine security and self-reliance and for joint procurement, price negotiations and information sharing are becoming more common and reporting successes.[14,15]

Supplies of some vaccines are at risk. While most vaccines are produced by four or more manufacturers, some vaccines have only one or two manufacturers.[4] This can lead to higher prices, increase the risk of supply interruptions and limit the ability to meet demand, especially for humanitarian response and short-term needs.

Role of innovation. Better capabilities for forecasting, procurement and supply will do more than address these challenges: they will also enable greater efficiency and impact through innovation. UNICEF's innovative phased tender approach is a striking example. In this approach, the total volume of pentavalent vaccine required for 2017–19 was tendered in two phases. Prices from the first phase were published, allowing manufacturers to adjust their pricing strategy for the second phase of the tender. This approach halved the weighted average price per dose for pentavalent vaccines, saving Gavi more than US$350 million over the tender period while maintaining supplier diversity and manufacturing capacity.[16]

Strategic interventions

Improve planning, forecasting and supply chain management. Multiple efforts are needed to improve demand forecasts, lowering risks for countries and manufacturers alike. These include strengthening of multi-year forecasting and budget-

ing as well as integration of immunization and wider health sector planning through national immunization strategies and related operational planning, as discussed in SP6 Sustainable Financing. Procurement staff are an essential part of the solution. Capacity building is needed to increase buyer competencies, professionalize vaccine procurement, and ensure procurement staff are appropriately recognized and compensated. This will improve the reliability of demand-planning processes and provide greater visibility in national immunization plans, including for vaccine introductions, vaccination campaigns and vaccine stockpiling. It will also highlight potential increases in demand due to contextual factors such as urbanization, migration and conflict.

Improving supply chain management will improve demand forecasts by creating feedback loops that align national forecasts with actual vaccine volumes ordered and stock on hand, yielding better logistics information. The WHO-UNICEF Effective Vaccine Management (EVM) initiative provides a comprehensive approach to help countries improve supply chain management. It sets minimum standards for vaccine and supplies management, defines quality indicators for every level of the supply chain and establishes a process of continuous quality improvement. EVM will continue to be central to global efforts to improve supply chain management.[17]

Finally, pooled procurement mechanisms such as those managed by UNICEF and PAHO should continue to engage in strategic, tactical and operational forecasting. Data are systematically collected from countries on their coverage, wastage and projected demand. These data are mapped against previous procurement activity to highlight changes in requirements. Forecasts are shared with suppliers to provide guidance on future requirements, including any shifts in country product presentation preferences, production and shipment plans, and variations in contracted quantities.

Strengthen learning and collaboration. Three networks are improving capabilities and strengthening collaboration in the vaccine supply ecosystem:

- **Technet-21** is a global network of immunization professionals who share experiences, coordinate activities and discuss developments in immunization. Discussion topics include vaccines and delivery technologies, supply chain and logistics, cold chain equipment, immunization information systems and coverage monitoring, service delivery, programme management, and global initiatives.[18]
- **The Vaccine Procurement Practitioners Network (VPPN),** hosted by UNICEF, is a network of senior procurement practitioners and technical experts. Members share expertise on market assessments, forecasting and planning, procurement strategies, tendering and contracting approaches, regulatory considerations, and industry needs and practices. Originally launched to serve middle-income countries, the VPPN will be expanded to serve all self-procuring countries. Data sharing by VPPN members will enhance the accuracy of global demand forecasts.
- **The Vaccine Market Dynamics Consortium (VMDC)** draws together key stakeholders to understand the changing needs of vaccine markets, identify shared challenges and consider ways to improve the health of vaccine markets. The VMDC includes donor groups, UNICEF and WHO, industry, civil society organizations and independent experts.

Provide technical assistance in procurement. UNICEF and WHO should enhance their technical support to other pooled procurement mechanisms, to self-procuring countries, and to cross-country collaborations to improve access to vaccines. To inform this support, WHO should comprehensively benchmark country procurement systems to identify areas where country systems are weak, such as health technology assessment, governance, regulatory processes, financing and access to market information. Support will also be informed by the market assessments discussed in Section 4.1.

Sources of assured quality vaccines

Strengthen regulatory capacity in all countries to improve timely access to vaccines of assured quality and to allow diversification of manufacturing sources.

Key evidence and gaps

Ensuring the safety and quality of all vaccines and addressing substandard and falsified medical products requires stable, well-functioning and integrated regulatory systems in the country of manufacture as well as in the countries where the vaccines are used. In 2018, 99% of the globally available doses of vaccines used in national immunization programmes were of assured quality, evidence of strong regulatory capacity in most vaccine-producing countries.[4] Despite assurance that vaccines meet global quality standards, DCVMs report that some countries are reluctant to procure products manufactured in developing countries.[19]

Conversely, many vaccine-importing countries lack the regulatory capacity needed to ensure the quality of imported vaccines. Some fail to coordinate regulatory and procurement processes, leading to sole supplier situations that can increase vaccine prices and the risk of stockouts. For example, in 2018 more than one-fifth of countries with Bacillus Calmette-Guérin vaccine (BCG) in their routine immunization schedules had only a single BCG product registered, or none at all, and did not accept vaccines on the basis of prequalification or facilitated procedures.[4]

Across countries, diverse legal provisions and regulatory requirements and weak regulatory capacity lead to registration delays and increased costs. Aligning registration procedures and requirements, and promoting mechanisms whereby well-established national regulatory authorities (NRAs) provide assistance to less mature NRAs, can facilitate access.[20] Regulatory oversight of distribution channels, post-marketing surveillance, and monitoring for falsified and substandard products are also needed to ensure safety and quality of all vaccines.

Some countries are exploring opportunities to begin or increase local production of vaccines as a way to improve the diversity of manufacturing sources and national or regional supply security. Countries that begin vaccine production will need to strengthen their regulatory capability to assure the quality of domestic products.

Strategic interventions

Regulatory capacity for all countries. WHO is providing technical guidance for vaccine regulators.[21] The WHO Global Benchmarking Tool is used to evaluate national regulatory systems and identify strengths and areas for improvement. It describes the overall "maturity level" of a regulatory system. This

enables Institutional Development Plans (IDPs) to be formulated to address gaps and assess progress in improving regulatory systems.[22]

WHO should continue developing regulatory guidelines and its capacity-building programme, including benchmarking regulatory systems, formulating IDPs, providing technical support and training, and convening networking and harmonization activities such as the African Vaccine Regulatory Forum. To ensure vaccine safety, it should also support countries to strengthen their capacity for pharmacovigilance, including post-marketing surveillance and safety and effectiveness evaluations, especially when new vaccines are introduced. In addition, countries should be encouraged to register a broader list of suppliers to improve supply security and sustain in-country competition.

Regulatory capacity in vaccine-producing developing countries. WHO is providing technical support to NRAs in vaccine-producing countries and in countries that are developing domestic capacity for vaccine production. WHO is supporting these countries to improve their capacity to provide oversight for newer, more complex vaccines and to rapidly evaluate new vaccines in emergencies.

Regulatory capacity and harmonization in vaccine-importing countries. Countries should be encouraged to remove barriers to harmonization, standardize registration processes and use facilitated regulatory pathways to accelerate access and minimize the burden on manufacturers and associated costs that affect vaccine prices. These may include legal arrangements to allow standing waiver of NRA approval for any WHO prequalified products. Ongoing mechanisms for regulatory harmonization and capacity building and facilitated regulatory pathways should be continued and strengthened. These include the harmonization of regulatory requirements and procedures such as through the International Council on Harmonization. They also include regional regulatory authorities and mechanisms whereby more mature NRAs provide assistance to those at lower maturity levels.

Enable diversification of manufacturing sources. WHO is providing technical assistance to countries exploring or beginning local production of vaccines. WHO's NRA strengthening initiative has played a major role in equipping countries to make vaccine regulatory decisions and assuring the quality of vaccines.

In addition, WHO administers two mechanisms that help countries to export vaccines, broadening the range of suppliers in the market. The first mechanism is a certification scheme for NRAs that provides assurance that they are functional and capable of applying the required regulatory oversight and standards to products within their authority.[23,24]

The second mechanism is the WHO Vaccine Prequalification programme, which ensures the quality, safety, efficacy and programmatic suitability of vaccines purchased by procurement agencies, including PAHO and UNICEF. Prequalification also provides assurance to countries that are procuring vaccines directly but may not yet have the capacity to make vaccine regulatory decisions on their own that products are safe, efficacious, programmatically suitable and of high quality. Prequalification requires a competent NRA that can provide effective oversight of product development, production and release processes, as well as ongoing monitoring to assure product quality and safety.[25]

Assumptions and risks: If greater harmonization in regulatory requirements and processes is not achieved, the perception of unequal regulatory standards, where one country is more stringent than another, will persist. Lack of confidence in the quality of vaccines manufactured by emerging suppliers may limit their ability to contribute to vaccine affordability and availability.

Supply for emergency situations

Strengthen mechanisms for rapid access in emergencies, outbreaks or pandemics and for people who require humanitarian aid. The mechanisms include sustainable manufacture and new means for rapid scaling-up of production to meet surge requirements.

Key evidence and gaps

In humanitarian emergencies, populations face increased risks of many infectious diseases. The governments and non-governmental organizations serving these populations face obstacles in obtaining sufficient supplies of affordable vaccines to prevent these diseases.[26]

Vaccine stockpiles are needed in some cases to ensure rapid access in the event of an outbreak or increased endemic transmission. The International Coordinating Group is managing emergency stockpiles of meningococcal, yellow fever and oral cholera vaccines, making equitable vaccine allocations through careful assessment of risk, and coordinating the use of limited amounts of vaccines.[27] Global vaccine stockpiles for smallpox and polio are managed by WHO and a consortium of agencies and experts in agreement with countries. Vaccines are secured through global supply agreements under rigorous regulatory and biocontainment policies and procedures and require approval of the WHO Director General before they are released.

Vaccine stockpiles can also speed responses to emerging pathogens. Stockpiles that are managed globally or by a consortium of countries can reduce the need for individual countries to manage their own national stockpiles for rare events. Stockpiling is especially applicable for vaccines that have achieved regulatory market authorization but are not currently recommended for routine programmes, such as Ebola vaccines.

For ***pandemic influenza,*** the Global Influenza Strategy 2019–2030 (GIS) calls for strengthening of pandemic preparedness and response for influenza. The Global Action Plan for Influenza Vaccines (GAP) has helped to build seasonal and pandemic vaccine production capacity. Through the GAP technology transfer initiative, 14 vaccine manufacturers in developing countries have received support to expand influenza vaccine production capacity.

Timely and equitable access to pandemic influenza vaccines will also depend on capacity within countries to regulate pandemic influenza products and to plan for influenza vaccine deployment. The Pandemic Influenza Preparedness (PIP) Framework is a global approach to pandemic influenza preparedness and response that is improving data and strain sharing for influenza viruses with human pandemic potential. It is also increasing the access of developing countries to vaccines and other pandemic

response supplies. In accordance with the PIP framework, 48 countries have implemented defined regulatory approaches that enable timely approval for use of pandemic influenza products and 24 countries have participated in simulation exercises to test the deployment of pandemic influenza vaccines and other products.[28–30]

Emerging infectious diseases demand rapid and efficient development and scale-up of new vaccines, as well as mechanisms to ensure equitable access. Capacity to do this should be built before a pandemic has struck.31 The Ebola outbreak in West Africa in 2014–15 led to concerted efforts across countries, development agencies and manufacturers. Global stakeholders shared development costs, collaborated on innovative trial designs and shared reputational risks to support accelerated availability of vaccines used in the Ebola outbreak in the Democratic Republic of the Congo in 2018–20.

The COVID-19 pandemic presents an even greater challenge. Multiple vaccine candidates are in development, but substantial at-risk investments are still needed to bring them to market and to manufacture them at huge scale to meet global needs. Once available, supply is expected to be limited and allocation strategies are not yet clear. A coherent strategy will be needed to shape this vaccine market into one that serves all countries, whatever their resources, capacities and needs. The Access to COVID-19 Tools Accelerator aims to bring stakeholders together to ensure equitable global access to innovative tools for COVID-19. Funding for vaccine research and development accompanied by requirements for global access and demand-side incentives such as advance market commitments can play an important role in ensuring global access.[32,33]

Strategic interventions

Secure vaccine supply for humanitarian emergencies. In 2013, "Vaccination in acute humanitarian emergencies: a framework for decision making" was developed by WHO, and in 2017 the WHO humanitarian mechanism was launched to meet urgent needs for vaccines in emergencies. Under this mechanism, multiple manufacturers have committed to supplying pneumococcal conjugate vaccine at a set price. Civil society organizations have purchased and deployed vaccine in humanitarian emergencies. WHO provides oversight, ensuring the appropriateness of the request, and UNICEF provides procurement support.

To achieve full impact, more manufacturers need to commit additional vaccines to the humanitarian mechanism and more organizations need to make use of the available vaccines. Credible demand estimates and clarity on requirements would allow manufacturers to factor humanitarian needs into their production and ensure they have sufficient reserve supplies to participate.[26,34]

Secure adequate supply for outbreak response stockpiles. Stockpile management should reflect both the recommended use of the vaccine and the public health objectives for the disease. Given the importance of disease prevention, emergency stockpiles should be sufficient to address most outbreak scenarios and risk–benefit decisions should prioritize minimizing vaccine shortages. Mitigating the risk of wastage should be an important but secondary consideration.

Stockpiles often face challenges in forecasting vaccine demand and securing affordable vaccines. Strategies to improve the management of these stockpiles must con-

sider how the vaccine is manufactured, as the lead times and production yields vary widely and affect how quickly a vaccine may be available. Market-shaping activities that address demand–supply challenges and improve the market dynamics may be needed to improve stockpile efficiency and sustainability.

In cases where a vaccine is primarily used for outbreak response, such as for meningococcal polysaccharide vaccines, the difficulty of forecasting outbreak size and frequency creates additional challenges in stockpile management. Because there are limited alternative uses for the vaccine, unexpectedly large outbreaks can lead to vaccine shortages, while outbreaks that fail to materialize can lead to wasted doses. These situations require risk mitigation strategies as well as risk-sharing between the buyer and supplier. Risks can also be eliminated by identifying alternative uses for the vaccines that provide more consistent demand, by stockpiling vaccines that are also appropriate for preventive use (such as meningococcal conjugate vaccines) or by implementing disease control strategies that prevent outbreaks, rendering the outbreak response stockpile unnecessary.

Establish regulatory mechanisms for emergencies. WHO has implemented the Emergency Use Listing Procedure for Candidate Vaccines for Use in the Context of a Public Health Emergency (EUL), which expedites the availability of candidate vaccines when there is no licensed vaccine available for the population in need.[35] Countries complement the EUL by monitoring the performance of products deployed under this procedure for safety, effectiveness and programmatic suitability. Transparency and data sharing for products under development will increase confidence in regulatory authorities responsible for protecting the health of their populations.

Prepare for the next influenza pandemic. The GIS and PIP will continue to support and drive improvements in access to pandemic influenza vaccines through expanding seasonal influenza prevention and control policies and programmes to protect the vulnerable; supporting timely access to quality-assured pandemic influenza products; and strengthening national, regional and global planning to enable timely and effective pandemic readiness.[28]

Enable rapid development and scale-up of new vaccines. For emerging infectious diseases, incentivizing and streamlining vaccine development, testing, licensure and manufacture at scale can improve equitable access to vaccines in emergency situations. This includes accelerating the response times for existing vaccine manufacturing platforms and developing technologies that can be rapidly taken to scale, such as DNA- and RNA-based vaccines. Modular manufacturing systems that can produce low-cost vaccines independent of scale or geography can also improve access. As noted above, expedited regulatory processes for clinical development of pandemic vaccines and for registration and importation to countries are also needed. These should ensure that candidates are shown to meet the performance and operational needs of all relevant settings, particularly low-resource settings.

The Coalition for Epidemic Preparedness Innovations (CEPI), which brings together researchers, manufacturers, regulators and affected countries, is funding, coordinating and enabling the development of new vaccines against priority infections.

This model could be applied to other needs in pandemic preparedness. Mechanisms to accelerate the development and scale-up of new vaccines should ensure equitable access to the products they support.

Assumptions and risks: For the COVID-19 pandemic, serious risks remain that vaccine supplies will be insufficient to meet global needs, and that the available doses will be distributed inequitably, leaving the most vulnerable unprotected. Global collaboration for rapid, fair access to safe and effective vaccines will be needed to control this pandemic.

Mechanisms to provide vaccines for emergencies must make it possible for manufacturers to engage sustainably. This is especially true for emerging infectious disease vaccines, given the substantial up-front investments needed to develop new vaccines and build manufacturing capacity and their unpredictable long-term commercial demand.

Resources

Innovation and affordability

- USAID Center for Innovation and Impact. Healthy Markets for Global Health: A Market Shaping Primer. 2014. Washington DC: USAID. Available at: https://www.usaid.gov/sites/default/files/documents/1864/healthymarkets_primer_updated_2019.pdf
- WHO. WHO's Preferred Product Characteristics (PPCs) and Target Product Profiles (TPPs). https://www.who.int/immunization/research/ppc-tpp/en/
- Gavi, the Vaccine Alliance. Supply and procurement roadmaps. https://www.gavi.org/our-alliance/market-shaping/supply-and-procurement-roadmaps.

Vaccine forecasting, procurement and supply

- UNDP. Public Procurement Capacity Development Guide. 2010. New York: UNDP. Available at: https://www.undp.org/content/dam/aplaws/publication/en/publications/capacity-development/undp-procurement-capacity-assessment-users-guide/Procurement%20Capacity%20Assessment%20Guide.pdf
- Arias D, Cashin C, Bloom D, Saxenian H, Wilson P. Immunization Financing: A Resource Guide for Advocates, Policymakers, and Program Managers. 2017. Washington DC: Results for Development. Available at: https://www.r4d.org/resources/immunization-financing-resource-guide-advocates-policymakers-program-managers/

Sources of assured quality vaccines

- WHO. Vaccine and immunization quality and safety. https://www.who.int/immunization/quality_safety/en/
- WHO. Increasing access to vaccines through technology transfer and local production. 2011. Geneva: WHO. Available at: https://www.who.int/phi/publications/Increasing_Access_to_Vaccines_Through_Technology_Transfer.pdf
- Plotkin S, Robinson JM, Cunningham G, Iqbal R, Larsen S. The complexity and cost of vaccine manufacturing - An overview. Vaccine. 2017;35(33):4064-4071. doi: 10.1016/j.vaccine.2017.06.003.

Supply for emergency situations

- WHO. Strengthening national emergency preparedness. https://www.who.int/activities/strengthening-national-emergency-preparedness
- WHO. Report of the Third WHO Consultation on the Global Action Plan for Influenza Vaccines (GAP) held in Geneva, Switzerland, 16-17 November 2016. 2017. Geneva: WHO. Available at: https://apps.who.int/iris/bitstream/handle/10665/259727/WHO-HIS-TTi-17.6-eng.pdf;jsessionid=5BAD5401AD9A27B399CE168B70ADFCAB?sequence=1
- Global Polio Eradication Initiative. Strategy for the Response to Type 2 Circulating Vaccine-Derived Poliovirus 2020-2021: An addendum to the Polio Endgame Strategy 2019-2023. 2020. Geneva: WHO. Available at: http://polioeradication.org/wp-content/uploads/2020/04/Strategy-for-the-response-to-type-2-circulating-Vaccine-Derived-Poliovirus-20200406.pdf

Bibliography

1. USAID Center for Innovation and Impact. Healthy Markets for Global Health: A Market Shaping Primer. 2014. Washington DC: USAID. Available at: https://www.usaid.gov/sites/default/files/documents/1864/healthymarkets_primer_updated_2019.pdf

2. Mihigo R, Okeibunor J, Cernuschi T, Petu A, Satoulou A, Zawaira F. Improving access to affordable vaccines for middle-income countries in the African region. Vaccine. 2019;37:2838-42. doi: 10.1016/j.vaccine.2019.03.077.

3. Pan American Health Organization. Call for a New Model of Coordination on Future Market Shaping Activities for COVID-19 Vaccine for All Countries Regardless of Income Strata: "Leaving No-one Behind". 2020.

4. WHO. Global Vaccine Market Report. 2019. Geneva: WHO. Available at: https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module2/2019_Global_Vaccine_Market_Report.pdf

5. WHO. WHO recommendations for routine immunization – summary tables. https://www.who.int/immunization/policy/immunization_tables/en/

6. WHO. Global Vaccine Market Report. 2018. https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/module2/MI4A_Global_Vaccine_Market_Report.pdf

7. WHO. Roadmap for access to medicines, vaccines and other health products 2019-2023. Comprehensive support for access to medicines, vaccines and other health products. 2019. Geneva: WHO. Available at: https://apps.who.int/iris/bitstream/handle/10665/330145/9789241517034-eng.pdf?ua=1

8. Malhame M, Baker E, Gandhi G, Jones A, Kalpaxis P, Iqbal R et al. Shaping markets to benefit global health - A 15-year history and lessons learned from the pentavalent vaccine market. Vaccine X. 2019;2:100033. doi: 10.1016/j.jvacx.2019.100033.

9. WHO. MI4A: Market Information for Access to Vaccines. https://www.who.int/immunization/programmes_systems/procurement/mi4a/platform/en/

10. UNICEF. UNICEF Pricing Data. https://www.unicef.org/supply/pricing-data

11. Ramirez Gonzalez A, Farrell M, Menning L, Garon J, Everts H, Hampton LM et al. Implementing the Synchronized Global Switch from Trivalent to Bivalent Oral Polio Vaccines – Lessons Learned From the Global Perspective. J Infect Dis. 2017;216:S183-S92. doi: 10.1093/infdis/jiw626.

12. Plotkin S, Robinson JM, Cunningham G, Iqbal R, Larsen S. The complexity and cost of vaccine manufacturing - An overview. Vaccine. 2017;35:4064-71. doi: 10.1016/j.vaccine.2017.06.003.

13. WHO. Multi-country Regional Pooled Procurement of Medicines. Identifying key principles for enabling regional pooled procurement and a framework for inter-regional collaboration in the African, Caribbean and Pacific Island Countries. 2007. Geneva: WHO. Available at: http://158.232.12.119/medicines/publications/PooledProcurement.pdf

14. WHO Regional Office for Europe. Cross-country collaborations to improve access to medicines and vaccines in the WHO European Region. 2020. Copenhagen: WHO. Available at: https://apps.who.int/iris/bitstream/handle/10665/332933/9789289055031-eng.pdf

15. Association of South-East Asian Nations (ASEAN). ASEAN Leaders' Declaration on ASEAN Vaccine Security and Self-Reliance (AVSSR). 2019. https://asean.org/storage/2019/11/7-ASEAN-Leaders-Declaration-on-ASEAN-Vaccine-Security-and-Self-Reliance-AVSSR.pdf

16. UNICEF Supply Division. Pentavalent vaccine (DTPwP-HepB-Hib): Market & Supply Update. 2017. New York: UNICEF. Available at: https://www.unicef.org/supply/media/541/file/Pentavalent%20vaccine(DTwP-HepB-Hib)%20market%20and%20supply%20update.pdf

17. WHO. Effective Vaccine Management (EVM) Initiative. https://www.who.int/immunization/programmes_systems/supply_chain/evm/en/

18. TechNet-21: The Technical Network for Strengthening Immunization Services. https://www.technet-21.org/

19. Pagliusi S, Ting CC, Khomvilai S, DCVMN Executive, Organizing Committee Group. Quality vaccines for all people: Report on the 16th annual general meeting of the Developing Countries Vaccine Manufacturers' Network, 05-07th October 2015, Bangkok, Thailand. Vaccine. 2016;34:3562-7. doi: 10.1016/j.vaccine.2016.02.067.

20. Dellepiane N, Pagliusi S, Regulatory Experts Working Group. Opportunities for improving access to vaccines in emerging countries through efficient and aligned registration procedures: An industry perspective. Vaccine. 2019;37:2982-9. doi: 10.1016/j.vaccine.2019.03.025.

21. WHO. Regulatory system strengthening for medical products (Sixty-seventh World Health Assembly agenda item 15.6). 2014. Geneva: WHO. Available at: https://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_R20-en.pdf

22. WHO. WHO Global Benchmarking Tool (GBT) for evaluation of national regulatory systems. https://www.who.int/medicines/regulation/benchmarking_tool/

23. Luter N, Kumar R, Hozumi D, Lorenson T, Larsen S, Gowda B et al. An updated methodology to review developing-country vaccine manufacturer viability. Vaccine. 2017;35:3897-903. doi: 10.1016/j.vaccine.2017.04.087.

24. WHO. National regulatory authorities (NRAs) and National Control Laboratories (NCLs) in countries producing vaccines prequalified for purchase by UN agencies. https://www.who.int/immunization_standards/national_regulatory_authorities/offices/

25. WHO. Vaccine PQ: Prequalification of Vaccines. https://www.who.int/immunization_standards/vaccine_quality/vq_index/en/

26. Elder K, Saitta B, Ducomble T, Alia M, Close R, Scheele S et al. Ensuring access to affordable, timely vaccines in emergencies. Bull World Health Organ. 2019;97:851-3. doi: 10.2471/BLT.18.228585.

27. WHO. International Coordinating Group (ICG) on Vaccine Provision. https://www.who.int/csr/disease/icg/qa/en/

28. WHO. Global influenza strategy 2019-2030. 2019. Geneva: WHO. Available at: https://apps.who.int/iris/bitstream/handle/10665/311184/9789241515320-eng.pdf

29. Global Action Plan for Influenza Vaccines (GAP) Advisory Group. The ten years of the Global Action Plan for Influenza Vaccines. 2016. Geneva: WHO. Available at: https://www.who.int/influenza/GAP_AG_report_to_WHO_DG.pdf?ua=1

30. WHO. Pandemic Influenza Preparedness Framework: Biennial Progress Report 1 January 2018-31 December 2019. 2020. Geneva: WHO. Available at: https://www.who.int/influenza/pip/PIP_Biennial_2018-2019.pdf?ua=1 [accessed May 28, 2020].

31. WHO. An R&D Blueprint for Action to Prevent Epidemics. 2016. Geneva: WHO. Available at: https://www.who.int/blueprint/about/r_d_blueprint_plan_of_action.pdf?ua=1

32. WHO. The Access to COVID-19 Tools (ACT) Accelerator. https://www.who.int/initiatives/act-accelerator

33. Silverman R, Krubiner C, Chalkidou K, Towse A. Financing and Scaling Innovation for the COVID Fight: A Closer Look at Demand-Side Incentives for a Vaccine. 2020. Washington, DC: Center for Global Development. Available at: https://www.cgdev.org/sites/default/files/Silverman-Krubiner-Chalkidou-Towse-R%26D-COVID.pdf

34. WHO. Vaccination in humanitarian emergencies. https://www.who.int/immunization/programmes_systems/policies_strategies/vaccination_humanitarian_emergencies/en/

35. WHO. Emergency Use Listing Procedure. 2020. Geneva: WHO. Available at: https://www.who.int/diagnostics_laboratory/eual/200110_new_eul_procedure_final.pdf?ua=1