



Working Towards a Sustainable, Healthy Market for Vaccines: a Comprehensive Framework to Support Policy Dialogue and Decision-Making

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Abbreviations

CEPI – Coalition for Epidemic Preparedness Innovations

Gavi – Gavi, the Vaccine Alliance

HVMF – Healthy Vaccine Market Framework

LIC – Lower-Income Country

LMIC – Lower Middle-Income Country

OECD – Organization for Economic Co-operation and Development

PAHO – Pan American Health Organisation

R&D – Research and Development

ROI – Return on Investment

USAID - US Agency for International Development

WHO – World Health Organisation

Executive Summary

Policymaking and market-shaping interventions aimed at enabling and sustaining a healthy global market for vaccines necessitate frameworks that reflect the unique needs, priorities, and risks across the supply- and demand-side of the global vaccines market. However, current frameworks that describe the global vaccines market are limited in scope, focusing largely on demand-side activities in low- and lower-middle income countries. Further, they do not fully reflect the interconnectedness of national and regional vaccine markets that comprise the global vaccines ecosystem, and they do not account for spill-over effects of market-shaping activities across markets and across time.

To provide a foundation for more comprehensive thinking, policy dialogue, and decision-making, there is a need for a healthy vaccines market framework (HVMF) that identifies: (i) specific characteristics of vaccines markets at the national, regional, and global level; (ii) dynamics that stem from individual supply- and demand-side activities; (iii) broad diversity of stakeholders that operate in and shape the vaccines markets; and (iv) resulting implications for enabling a healthy market.

The Healthy Vaccines Market Framework (HVMF)

Building on existing literature, the HVMF aims to provide a comprehensive overview of the components and functioning of the global vaccines market that illustrates how key characteristics of a healthy vaccines market are shaped by the actions and decisions of supply- and demand-side stakeholders. Moreover, this paper depicts how challenges in the global vaccines market may be rooted in multiple factors across the market, and how market-shaping interventions aimed at addressing a single challenge in an individual country can have unintended effects on vaccine markets across countries and both in the short- and long-term. By expanding upon the breadth and depth of existing frameworks, the HVMF seeks to promote and encourage strategic and collaborative dialogue and more informed decision-making across stakeholders in the global market.

The central goal of a healthy vaccines market is to address public health needs through sustainable innovation and equitable access. The HVMF identifies four essential characteristics of a healthy vaccines market: (i) balanced supply and demand; (ii) affordability and return on investment (ROI); (iii) product innovation and quality; and (iv) sustainable buyer and supplier risk. Another key feature of the HVMF is that it draws attention to the diverse set of stakeholders that are actively engaged in the vaccine ecosystem and market-shaping activities at the national, regional, and global level. Given this complex set of dynamics, it is critical that all actors shaping the global vaccines market understand the broader implications and interconnectedness of individual supply- and demand-side activities and how they shape the global marketplace collectively.

Case study analysis: COVID-19 vaccines

We used a case study approach to demonstrate HVMF's utility in describing supply- and demand-side challenges across the vaccines market. The case study identifies how specific market-shaping interventions used to address these challenges impact the characteristics of a healthy market directly or indirectly across national, regional, and the global vaccines market. While different challenges within the global vaccines market were considered, we selected recent efforts to accelerate and scale-up the development and manufacturing of COVID-19 vaccines in response to the pandemic and provide examples of their potential impact in the short- and long-term. The case study drew from existing peer-reviewed and grey literature, as well as the authors' experiences with, and analysis of, the current landscape as it relates to the case study.

1 Introduction

The SARS-CoV-2 pandemic underscores the pivotal role vaccines play in disease prevention across the globe. It also brings to light the complexity of developing, manufacturing, and deploying vaccines. A well-functioning (i.e., healthy) global vaccines market is essential to enable sustained vaccine innovation and to promote equitable access needed to meet current and emerging public health threats. Maintaining a healthy market for vaccines requires a balance across supply- and demand-side factors, considering the different situations into which the vaccines market responds to market signals. Upstream, this necessitates a policy environment that enables resource-intensive research, development, and manufacturing capacity required to create a reliable, quality supply of vaccines. Downstream, reliable systems and infrastructure are required to ensure predictable demand, as well as efficient delivery through national immunisation programs to reach large cohorts of the population and ensure vaccines and vaccination programs reach their full potential.

Achieving a healthy vaccines market and balancing needs across both the supply- and demand-side is challenging. Unmet needs or gaps in the prevention of infectious diseases worldwide are indicative of this difficulty. On the demand side, underinvestment in vaccination programs contributes to insufficient access to vaccination services and uptake of vaccines. For example, total public spending on vaccination has been relatively flat among low and lower-middle income countries and is a small percentage (<0.5 percent) of total spending on health among Organization for Economic Co-operation and Development (OECD) countries (Xu et al., 2018). In many countries, insufficient internal processes and policies can contribute to delays in procurement, poor forecasting, and inappropriate stock management, as well as vaccine stock-outs (Lydon et al., 2016). The case for continued investment and access to new vaccines is hindered by narrow assessment frameworks and insufficient data systems that are unable to evaluate the full societal value of vaccination (Bärnighausen et al., 2014; Hollingsworth et al., 2020).

On the supply side, vaccine development and manufacturing are global endeavours that are intricately linked to policies, systems, and infrastructure spanning across countries and stakeholders. Risks (i.e., upfront investment, scientific uncertainty, and opportunity costs) associated with research and development (R&D) for companies necessitates policies, investors, and investment models that enable and reward innovation (Serdobova and Kieney, 2006; Hemel and Ouellette, 2019). The nature of the global vaccine supply chain warrants supply-side stakeholders to create supply chain resiliency to secure manufacturing and delivery of their products (Lee and Haidari, 2017). Lastly, global vaccine supply and access strategies are informed by national recommendations, demand forecasts, pricing policies, and procurement mechanisms across countries. As such, market-shaping activities at the national level cannot be viewed in isolation and can have a broader knock-on effect at the regional or global level. This, subsequently, may enable or hinder innovation, timely development, and stable supply of successful vaccine candidates. Such challenges on both the supply- and demand-side of the global vaccines market necessitate greater dialogue and collaboration across the vaccine ecosystem.

This paper presents a conceptual framework for a healthy vaccines market, developed for application at the national, regional, and global level to facilitate dialogue across all stakeholders on the implications of market-shaping activities. Building on existing literature, the proposed Healthy Vaccines Market Framework (HVMF) aims to support comprehensive and inclusive thinking about healthy market dynamics. This paper also describes the potential intended and unintended effects of specific activities on vaccine stakeholders, as well as on vaccine markets across countries in the short- and long-term.

2 Methods

We performed a literature review, refined, and validated by expert interviews, and used a case study approach to illustrate the HVMF's utility within a specific context.

2.1 Literature Review

The targeted literature review used the "snowballing" approach to identify peer-reviewed and grey literature describing healthy markets for vaccines and medicines. This involved selecting a key paper as a starting point and then checking reference lists both 'backwards' (i.e., the papers cited by the article of interest) and 'forwards' (i.e., any papers that have cited the article of interest). The US Agency for International Development's (USAID) Center for Accelerating Innovation and Impact's Market Shaping Primer served as the primary source for the literature search. This paper describes the "state of practice" of market-shaping activities to increase access to life-saving commodities. Addressing both the vaccines and medicines market, it assesses market-shaping activities within the context of reducing long-term demand and supply imbalances to reach a sustainable equilibrium.

Healthy market frameworks identified during the literature review were then analysed to identify key characteristics, strengths, and limitations. From the analysis of identified papers, the following topics emerged: (i) market elements; (ii) focus (vaccines or general); (iii) geographic scope (according to World Bank classification by income level); (iv) perspective (supplier, buyer, other); and (v) aim of the framework (descriptive or analytic). Drawing from these findings, we developed a draft conceptual framework specific to vaccines that was then presented to experts for feedback.

2.2 Expert Interviews

Expert interviews were used to inform the initial design of the conceptual framework. A sample of experts (n=10) from academia and the pharmaceutical industry were selected based on their expertise in one or more of the identified categories: (i) public health; (ii) vaccine policy and economics; (iii) vaccine markets; and (iv) regulatory affairs. In-depth interviews consisted of open-ended questions focusing on the theoretical soundness, comprehensiveness, clarity, and applicability of the conceptual framework to support stakeholder collaboration. A narrative analysis approach was used to identify key insights, inform the final framework, and ensure the integrity of the case study.

2.3 Case Study Analysis

We used a case study approach to demonstrate HVMF's utility in describing supply- and demand-side challenges across the vaccines market. The case study identifies how specific market-shaping interventions used to address these challenges impact the characteristics of a healthy market directly or indirectly across national, regional, and the global vaccines market. While different challenges within the global vaccines market were considered, we selected recent efforts to accelerate and scale-up the development and manufacturing of COVID-19 vaccines in response to the pandemic and provide examples of potential impact in the short- and long-term. The case study drew from existing peer-reviewed and grey literature, as well as the authors' experiences with, and analysis of, the evolving landscape as it relates to the case study.

3 Results

3.1 Existing Frameworks

From the literature search, four key frameworks emerged for healthy markets. These frameworks helped inform the conceptual HVMF and were developed by Unitaid/Global Fund (The Global Fund, 2015), USAID (USAID, 2014), Gavi¹ (BMGF, UNICEF and GAVI, n.d.), and UNICEF (UNICEF, 2018). A summary of each framework is provided in Table 1 in the Appendix.

3.2 Healthy Vaccines Market Framework

The goal of a healthy vaccines market, as defined for this study, is to support sustainable innovation and equitable access in order to address public health needs. A visual representation of the HVMF is shown in Figure 1 with the goal depicted at the centre.

The conceptual framework is comprised of three parts that represent dependencies within a vaccines market: (i) specific characteristics of vaccines markets at the national, regional, and global level; (ii) supply- and demand-side activities and corresponding policies that drive these characteristics; (iii) the broad diversity of stakeholders that operate in and shape vaccines markets.

Five characteristics of a healthy vaccines market

The HVMF is based on four essential characteristics of a healthy vaccines market that are depicted within the central circle of Figure 1: (i) balanced supply and demand; (ii) affordability and return on investment (ROI); (iii) product innovation and quality; and (iv) sustainable buyer and supplier risk. We describe these four characteristics and illustrate their centrality to the HVMF in Table 2 in the Appendix.

National, regional, and global vaccines markets

The concentric circles around the centre of the framework illustrate that national, regional, and global vaccines markets are interconnected and do not operate in isolation. A national vaccines market, in this study, is defined as when the licensure, purchase, and delivery of a vaccine involves a single country, while a regional market groups together two or more countries to engage in these decisions and activities. We define the global vaccines market as encompassing national and regional markets.

Key activities influencing the vaccines market

Key supply- and demand-side activities that influence the health of the vaccines market are listed on the left-hand and right-hand side of the HVMF, respectively; activities are described in Table 3 and Table 4 in the Appendix. This list of activities is not intended to be exhaustive, rather draw attention to supply- and demand-side actions that have a significant impact on global vaccine market dynamics.

¹ Gavi's healthy markets framework was developed in conjunction with UNICEF and the Bill & Melinda Gates Foundation.

Key stakeholders in the vaccines market

At the top of the framework, we list key stakeholders and indicate whether they primarily influence demand- or supply-side activities, or both. Through their actions described in the HVMF, these stakeholders collectively determine the functionality, scope, and size of a vaccines market. On the demand side, self-procuring governments in high- and middle-income countries around the world constitute the largest segment of the vaccines market (60 percent of total volume and 93 percent of total value) (WHO, 2019). In addition, institutions such as UNICEF, Gavi, and the PAHO Revolving Fund who support procurement on behalf of other countries, particularly low and lower-middle income countries, also shape regional and the global vaccines market. On the supply side, vaccine research, development, and manufacturing are dominated by four major R&D multi-national manufacturers comprising 90 percent of global market share by value (not including COVID-19 vaccines) (WHO, 2020). By volume, five manufacturers dominate the market (WHO, 2020). This concentration results in part from high market entry costs, as well as relatively high R&D and production costs (Pronker et al., 2013). The remainder of global market value is comprised of an active biotechnology sector and other private and public vaccine manufacturers largely from developing countries and emerging markets. The response to the COVID-19 pandemic has brought new entrants to the global vaccine market, and this landscape will continue to evolve.

In addition, several other actors influence the supply- and demand-side of the vaccines market. These include global stakeholders such as the World Health Organization (WHO), the Coalition for Epidemic Preparedness Innovations (CEPI), and the Bill and Melinda Gates Foundation. These stakeholders make investments, provide technical guidance, or provide recommendations for specific types of vaccine markets (e.g., a target disease area or geography). Lastly, health care providers and consumers play a central role in the vaccines market by shaping demand through the administration and uptake of vaccines, respectively.

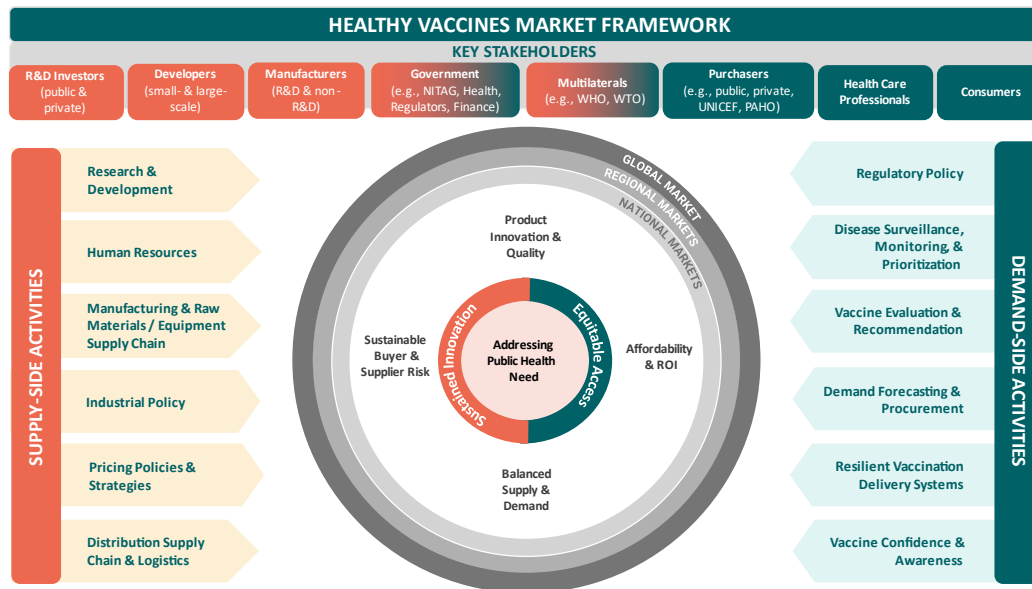


FIGURE 1. HEALTHY VACCINES MARKET FRAMEWORK

4 Case Study Analysis

This case study examines efforts to accelerate the development and scale-up manufacturing of COVID-19 vaccines. We demonstrate the utility of the HVMF by using it to identify shortcomings within the current global vaccines market, illustrate the interdependencies of supply- and demand-side actions, as well as understand potential knock-on effects of market-shaping interventions (USAID, 2014). Further, while the case study applies the framework to a unique situation (i.e., COVID-19 vaccines), we posit that this case study helps to underscore the need for the HVMF and that lessons learned from this are applicable across the vaccines market at the national, regional, and global level.

Vaccine production is a complex multistep process that must comply with local regulatory standards in each national market; the process involves hundreds of quality controls, adequate infrastructure, a global supply chain, and highly skilled workforce (Vaccines Europe, n.d.). Moreover, it has been estimated that it costs anywhere from \$50 million to \$700 million to build and prepare a plant to manufacture a new vaccine (Plotkin et al., 2017). Given this, manufacturers typically begin to invest capital into production infrastructure only once vaccine candidates pass certain stages of clinical development (i.e., proof-of-concept), and they have clear signals of public health need and market demand. In most instances, decisions to invest in new manufacturing capacity to increase future supply requires a long-term view of the market and is, therefore, particularly sensitive to the health of the global market altogether.

To meet the world's urgent need for COVID-19 vaccines, significant efforts are underway to bolster the current global manufacturing capacity and cut timelines for development and manufacturing (Lupkin, 2021). Prior to the pandemic, manufacturers produced roughly 5 billion doses of vaccines globally each year (including 1.5 billion influenza vaccines) (The Economist, 2020). As of August 2021, almost 5 billion doses of COVID-19 vaccines have been administered worldwide (Bloomberg, n.d.).

The urgent global demand for COVID-19 vaccines has driven a multi-faceted approach to ensure accelerated production at an unprecedented scale. National, regional, and global stakeholders have been implementing policies and interventions, including: (i) partnerships and push funding to leverage existing assets and offset financial risk to developers; (ii) demand forecasting and advanced purchase commitments to provide market predictability and stability; (iii) regulatory collaboration and streamlining processes to create efficiencies, optimise global supply chains, and reduce timelines. Drawing on the HVMF, these challenges and market-shaping efforts are associated with several supply- and demand-side activities and involve stakeholders across the ecosystem. Depending on the design and implementation of these interventions, they can affect the overall health of the vaccines market, including the supply of and access to other vaccines.

First, a range of strategic partnerships has sought to bring together the necessary expertise, assets, and resources to advance the development and manufacturing of COVID-19 vaccine candidates. Industry collaborations across industry and with academia or small biotechnology companies facilitate early-stage R&D and large-scale clinical trials, as well as manufacturing and distribution. These collaborations depend not only on industry's expertise and assets, but their ability to take on financial risk and make a series of investments as vaccine candidates advance. The current approach for COVID-19 vaccines is to scale-up manufacturing in parallel with clinical development. While necessary to accelerate timelines in the short run to respond to the pandemic, this approach is typically not efficient, risking the potential for imbalanced supply and demand, and sunk costs from idle manufacturing capacity (Billington et al., 2020). To help offset these risks, push funding is being provided through ad-hoc public-private partnerships with government bodies (e.g., the US Biomedical

Advanced Research and Development Authority or the European Commission) or global institutions (e.g., CEPI). In this capacity, these institutions operate as investors and must consider not only how they offset risk, but also other market characteristics such as their role in enabling innovation, ROI, and strong competition over time. As such, funding mechanisms that enable industry to continue product lifecycle management activities and allow tangible assets to be utilised once the immediate needs for COVID-19 vaccine manufacturing have been met can protect the health of the market in the longer-term (Lurie et al., 2020; HHS, 2017).

While push funding helps address upfront capital investment challenges, demand forecasting and pull funding can provide greater market predictability and stability in the face of an evolving pandemic. Due to long lead times required for vaccine manufacturing, accurate demand forecasting and aligning manufacturing priorities with forecasts are fundamental to ensuring stable supply. Globally, gaps in data systems (e.g., disease surveillance, immunisation information systems) and long-term planning result in inaccurate demand forecasts even for routine vaccines (Kaufmann et al., 2011). For COVID-19 vaccines, the uncertain and evolving epidemiology of the pandemic combined with the time and required supply resources to meet unparalleled global demand has sparked international dialogue and coordination to firm up demand forecasts, and to support allocation, procurement, and distribution. Typically, access strategies are tailored to country contexts, require data-intensive assessments, involve time-intensive procurement processes, and hinge on clear long-term local and global market outlooks for manufacturers. To accelerate access pathways, reduce buyer and supplier risk, and procure timely supply, global institutions and governments have been utilising pull funding – both advance market commitments² and advance purchase agreements³. The most notable effort for COVID-19 vaccines is the COVAX Facility, a unique collaboration to coordinate global allocation and procurement during the pandemic (Gavi, 2020a; Gavi, 2020b). While current pull funding mechanisms provide an immediate solution during the pandemic, they involve ad hoc regulatory, financing, and procurement policies for purchasing countries. Further, as they deviate from traditional commercial models for routine vaccines, stakeholders must also understand how they could influence market characteristics in the long-term, including fostering innovation, enabling ROI, and reducing buyer and supplier risk.

Lastly, accelerating production of COVID-19 vaccines has necessitated greater regulatory cooperation and streamlining of processes across vaccine markets to create efficiencies and optimise global supply chains. Manufacturing facilities, equipment, and processes require approval by regulators from each country or jurisdiction in which the vaccine will be administered. Regulatory requirements vary by country, and manufacturers and suppliers of auxiliary supplies (e.g., glass vials) may need to recalibrate manufacturing processes depending on geographic demand. Even the slightest process change, for example, a change in packaging or labelling, can interrupt the entire supply chain and result in delays in production and delivery. Reallocation of vaccine doses manufactured for one country to another country is, therefore, difficult if not impossible due to differences in regulatory requirements and images. Thus, further global cooperation by regulators, as well as harmonisation and streamlining of both pre-approval and post-market regulatory requirements will continue to be fundamental for facilitating rapid availability and access while maintaining the highest levels of safety, quality, and efficacy for COVID-19 vaccines. Unifying bodies, like the WHO through its prequalification process and the International Coalition of Medicines Regulatory Authorities, play an important role in enabling supply-side efficiency by issuing guidance and establishing global frameworks that can be applied across markets. Such efforts are critical for COVID-19 vaccines and can also have a long-term beneficial impact for all vaccines.

² Advance market commitments are where public or private donors make funding commitments to vaccine manufacturers and, in exchange, companies sign a legally-binding agreement to provide vaccines at an affordable price to low- and middle-income countries.

³ Advance purchase agreements are bilateral agreements between governments and manufacturers where governments agree to purchase a specific number or percentage of vaccines at a pre-negotiated price.

5 Discussion

The HVMF developed in this study aims to depict how the characteristics of a healthy vaccine market hinge on supply- and demand-side activities, as well as policies that cut across multiple markets. It helps illustrate how challenges in the global vaccines market may be rooted in multiple factors across a market, and how market shaping interventions aimed at addressing a single challenge in a single market can strengthen or undermine the overall health of the global vaccines market in the short- and long-term. Another key component of the HVMF is that it draws attention to the diverse set of stakeholders that are actively engaged in market-shaping activities at the national, regional, and global level. Given this complex set of dynamics, it is critical that all actors shaping the global vaccines market understand the broader implications and interconnectedness of individual supply- and demand-side activities and how they shape the global marketplace collectively.

The case study illustrates that the HVMF provides a tangible framework to aid in stakeholder understanding of what is needed to achieve a healthy vaccines market. The COVID-19 vaccines being developed today are the result of a global market that fosters innovation, and of the synchronised efforts of both supply- and demand-side stakeholders that are essential to uphold key healthy market characteristics at the national, regional, and global level. Vaccine research, development, and manufacturing requires substantial financial and technical resources, entails significant risk, and is shaped by demand-side signals and activities globally. A healthy market must balance risk, provide the right incentives to attract manufacturers, investors, and other supply-side stakeholders, as well as support sustainable financing models for both supply- and demand-side stakeholders. Incomplete demand forecasts or unclear market outlooks can contribute to manufacturer uncertainty and cause supply to fluctuate between product excess and shortage. Access strategies and procurement models that seek to accelerate availability and create market stability in the short-term should ensure that such interventions do not disrupt long-term market viability at the national, regional, and global level. Regulatory processes should promote process innovation and manufacturing quality, and reduce cumbersome, disjointed processes that discourage manufacturers from seeking product registration and approval. These issues stress that risk-sharing interventions at the national, regional, and global level, in addition to broader collaboration across stakeholders on both sides of the HVMF, are crucial to promoting long-term market health for both pandemic and routine vaccines. Further, these issues underscore that market interventions should be evaluated and re-evaluated over time to ensure relevancy to market needs, and to understand the potential unintended consequences on the market over time. As the pandemic subsides and the epidemiology of COVID-19 shifts, the policies and interventions leveraged to respond to the pandemic may no longer be necessary. Stakeholders should work together to promote the health of the vaccines market.

Our research and resulting framework have limitations. First, while the snowballing approach is particularly useful for interdisciplinary topics where evidence may be scattered across databases, we did not intend to conduct a comprehensive literature review that identified all relevant papers. Rather, we focused on those that described a market framework most relevant to our research aims. Second, the number of non-industry experts interviewed was limited; however, given existing frameworks do not sufficiently describe supply-side activities, we felt it was important to place emphasis on individuals within this area of expertise. Third, the HVMF is positioned as a conceptual framework, not an analytical framework meaning it provides structure for systematic thinking versus a standardised market analysis. Fourth, the HVMF definition of a national vaccine market focuses on the point of regulatory approval and sale of a vaccine, and does not take into consideration that markets also play a role in the vaccine supply chain and the provision of raw materials, ancillary supplies, and other necessary components for vaccine development and manufacturing. While these markets are recognised as contributing to the global market, they are not the primary unit of analysis comprising the overall global vaccines market and, as we have seen during COVID-19, the input

supply market dynamics can create significant bottlenecks in the manufacturing process and potentially lead to production delays. Finally, the HVMF does not include a comprehensive set of activities and stakeholders, nor does it specifically call out the immediate and delayed impact of market shaping activities over time. The vaccine landscape is complex, evidence should be sought on a case-by-case basis, and generalisations should not be made across market shaping activities, market levels, or over time.

6 Conclusion

The HVMF can promote and encourage strategic and collaborative dialogue across the global market by expanding upon the breadth and depth of existing frameworks. Its goal is to advance the understanding of the downstream impact caused by individual market-shaping activities and how these activities work together to strengthen or degrade the health of vaccines markets over time. Furthermore, to maintain market health in the short- and long-term, its utility can be applied to anticipate market shortcomings and provide timely, sustainable interventions at the systems level. The COVID-19 pandemic, by placing a strain on health care systems and the global economy, shows the need to understand the supply- and demand-side aspects of a healthy vaccines market more comprehensively to better meet public health demand over time and across dynamic market events. In doing so, we can ensure that vaccines realise their full potential and are supported by a global market that promotes future growth, equitable access, and sustained innovation.

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Appendix

APPENDIX TABLE 1: SUMMARY OF EXISTING FRAMEWORKS FOR HEALTHY MARKETS

	UNITAID/GLOBAL FUND (THE GLOBAL FUND, 2015)	USAID (USAID, 2014)	GAVI ⁴ (BMGF, UNICEF AND GAVI, ND.)	UNICEF (UNICEF, 2018)
<i>Healthy market characteristics</i>	<ul style="list-style-type: none"> • Innovation • Availability • Demand and adoption • Quality • Affordability • Delivery 	<ul style="list-style-type: none"> • Affordability • Availability • Assured Quality • Appropriate Design • Awareness 	<ul style="list-style-type: none"> • Supply meets demand and country preferences • Additional supply security attributes: buffer capacity, individual supplier risk, NRA • Positive system features: total system effectiveness, long term competition, product innovation 	<ul style="list-style-type: none"> • Availability • Affordability • Competition • Quality • Acceptability/adaptability • Delivery • Funding security
<i>Focus (vaccines or general)</i>	General	General	Vaccines	General
<i>Geographic scope</i>	LICs and LMICs	LICs and LMICs	LICs and LMICs	LICs and LMICs
<i>Perspective (supplier or buyer)</i>	Buyer and supplier	Buyer and supplier	Buyer and supplier	Buyer and supplier
<i>Aim (descriptive or analytical)</i>	<i>Descriptive:</i> To arrive at a common definition of optimal market conditions to support health outcomes.	<i>Analytical:</i> To assess whether and how interventions may be appropriate for a specific underperforming market. The pathway begins by assessing the current health of the market and moves on to identifying market shortcomings that limit health impact.	<i>Analytical:</i> To have a common way of thinking about market health, to better communicate how to assess individual vaccine markets and their ability to best meet the needs of Gavi countries, and to improve how potential trade-offs between different market attributes are analysed.	<i>Descriptive:</i> To provide a market dashboard for assessing market shortcomings and opportunities for intervention.

⁴ Gavi's healthy markets framework was developed in conjunction with UNICEF and the Bill & Melinda Gates Foundation.

APPENDIX TABLE 2: FOUR CHARACTERISTICS OF A HEALTHY VACCINES MARKET

CHARACTERISTIC	DEFINITION AND ILLUSTRATIVE EXAMPLES
<i>Balanced Supply and Demand</i>	A healthy market should deliver appropriate and timely supply to meet predictable demand in addition to potential fluctuations. Advanced demand forecasting and planning are central to achieving this balance, along with early and open engagement across all stakeholders to allow manufacturers to optimise capacity and provide reliable supply (Vaccines Europe, 2016a). Several factors, including manufacturing cycles that average 2 years or more [Vaccines Europe, 2016b), changes in policies (e.g., new product regulations), events that influence demand for a vaccine (e.g., outbreaks), or unanticipated departure of a manufacturer from the marketplace, can result in supply interruptions that can last for extended periods of time.
<i>Affordability and Return on Investment</i>	In a healthy market, vaccines should be affordable to enable access, while also contributing to the ROI necessary to sustain innovation. Manufacturing, regulatory, pricing, procurement, and financing strategies and decisions by purchasers and suppliers impact both affordability and ROI. Affordability varies by country and depends on country priorities, willingness, and ability to pay based on budget allocation. For investors and manufacturers, ROI means profitability and ensuring a return on the costs of R&D, manufacturing, and commercial operations. For governments, ROI includes broad benefits of vaccination such as averted health-care costs or greater workforce productivity.
<i>Product Innovation and Quality</i>	A healthy market should consist of policies that ensure product quality and both incremental and breakthrough innovation across the biopharmaceutical sector, including across private, academic, government, and non-profit institutions. ⁵ Policies that foster, incentivise, and reward innovation, include intellectual property (IP) protections and non-IP policies such as grants, prizes, or tax credits that are set by governments, as well as by non-governmental institutions (Hemel and Ouellette, 2019). Criteria used to evaluate and procure vaccines also set standards for quality and promote innovation. Rewards for innovative and quality products can also stimulate healthy competition between existing suppliers and potentially attract new entrants.
<i>Sustainable Buyer and Supplier Risk</i>	In a healthy market, buyers and suppliers should be able to absorb some level of financial risk, however risk beyond a certain threshold can result in market exit. For example, an unpredictable market with unclear demand signals, or a highly price sensitive market with excessive downward pricing pressure can create too much risk and uncertainty for supply-side stakeholders to invest in development and manufacturing of a vaccine and may even result in market exit. For buyers, risk may present as supply uncertainty and concern as to whether a supplier will be able to deliver purchased doses. Thus, sustainable risk allows existing suppliers and buyers to remain active in the market and maintain healthy competition resulting in continued investment in R&D and manufacturing on the supply-side and the delivery of immunisation services on the demand-side. Sustainable risk may also encourage new entrants in the market, thus incentivising competition.

⁵ Incremental innovation may include a product profile that reduces cold chain requirements, is more easily administered in remote settings, has greater durability, or has safety data for use in children. Breakthrough innovation may include new platform technologies that enable rapid development and manufacturing of novel vaccines to rapidly respond to emerging infectious disease outbreaks.



APPENDIX TABLE 3: DEFINITIONS AND ILLUSTRATIVE EXAMPLES OF SUPPLY-SIDE ACTIVITIES

SUPPLY-SIDE ACTIVITIES	DEFINITION AND ILLUSTRATIVE EXAMPLES
Research & Development	Encompasses research from early-stage discovery through clinical development conducted by a variety of stakeholders, including academia, small biotech firms, and large-scale biopharmaceutical companies. Also includes actions primarily undertaken by investors, R&D-based manufacturers, governments, or other stakeholders to support policies, practices, or platforms to stimulate vaccine R&D. Examples may include partnerships between biotech firms and large-scale manufacturers to accelerate new vaccine candidate R&D, or publicly funded academic research grants to support basic science research.
Human Resources	Actions primarily undertaken by governments, manufacturers, or other stakeholders to ensure a workforce with the necessary specialised knowledge and skills to produce vaccines. Examples may include grants to encourage more students to pursue science and engineering degrees, or on-the-job training programs for example undertaken by manufacturers.
Manufacturing & Raw Materials / Equipment Supply Chain	Actions primarily undertaken by manufacturers to maintain or increase their capacity to meet demand. Examples may include upgrading manufacturing equipment to accelerate vaccine production, or diversifying suppliers of key raw materials and equipment used in manufacturing to mitigate supply chain risk. May also include policies and actions taken by governments to strengthen manufacturing capacity and supply chain resilience in the interest of national or health security.
Industrial Policy	Encompasses public policies primarily created by governments to stimulate the biopharmaceutical and life sciences sector. Also includes actions undertaken by other stakeholders such as multilateral organisations (e.g., World Trade Organization) and manufacturer trade associations (e.g., IFPMA) to inform corresponding policies. Examples include establishing policies on technology transfers or intellectual property protections.
Pricing Policies & Strategies	Actions taken by several stakeholders, including manufacturers, who determine price based on costs, value to society, demand, competition, and access. These stakeholders may also use pricing strategies such as tiered pricing or value-based pricing, as well as contracting mechanisms such as volume guarantees or multi-year contracts to achieve optimal price, access, and reduce market risk. Further, price and pricing strategies are informed by government and other payer policies regarding price and procurement that may seek to control costs or incentivise competition and innovation.
Distribution Supply Chain & Logistics	Actions that contribute to the ability of a supply chain to receive, store, distribute, and manage vaccines and their ancillary products. This includes distributing vaccines from port of entry to vaccination sites, in addition to proper quality, safety, and tracking mechanisms. Includes capabilities and capacity of both supply-side stakeholders such as manufacturers, as well as demand-side stakeholders such as government agencies or health systems managing immunisation programs.



APPENDIX TABLE 4: DEFINITIONS AND ILLUSTRATIVE EXAMPLES OF DEMAND-SIDE ACTIVITIES

DEMAND-SIDE ACTIVITIES	DEFINITION AND ILLUSTRATIVE EXAMPLES
Regulatory Policy	Actions primarily undertaken by national government or regional (e.g., European Medicines Agency) regulatory authorities to set standards for quality and safety both pre- and post-licensure of products. Also includes actions undertaken by global institutions such as the WHO (e.g., prequalification of vaccines), as well as actions undertaken by supply-side stakeholders such as manufacturers who comply with regulatory policies to ensure quality and safety. Examples include monitoring of efficacy and safety data during clinical trials or establishing good manufacturing practices.
Disease Surveillance, Monitoring, & Prioritisation	Actions primarily undertaken by governments, health systems, academic, and other institutions to oversee, monitor, and prioritise diseases to help countries better understand disease burden and epidemiology to inform vaccine policy and strategy.
Vaccine Evaluation & Recommendation	Actions primarily undertaken by governments and national immunisation technical advisory groups to assess and determine the value of vaccines and vaccination as well as how they are prioritised and recommended for implementation. Examples include recommendations for new vaccine introductions or decisions pertaining to funding or reimbursement of vaccines and vaccination services.
Demand Forecasting & Procurement	Actions primarily undertaken by governments and other institutions to determine volume of vaccines required (including purchase and reimbursement) for national immunisation programs, for strategic stockpiles, or to address outbreaks. Also includes actions taken by other stakeholders such as third-party buyers who may be involved in supporting procurement and supply-side manufacturers who use forecasts to plan for appropriate manufacturing capacity and pricing strategies.
Resilient Vaccination Delivery Systems	Actions primarily undertaken by governments to invest in and strengthen vaccination programs and systems to effectively and efficiently deliver vaccines and facilitate equitable access. This includes overseeing where vaccination services are delivered (e.g., clinical or non-clinical settings) and who administers vaccinations (e.g., pharmacists or other non-physician health providers), as well as the data systems necessary to monitor the delivery of vaccination services and corresponding coverage rates. Further, this includes ensuring the necessary resources – financial and human – are available to sustain vaccination programs and services at a sustainable level. Also includes action undertaken by multilaterals or other institutions who may also invest in or provide technical support to improve healthcare infrastructure.
Vaccine Confidence & Awareness	Actions undertaken by several demand-side, as well as some supply-side stakeholders across the vaccine ecosystem to promote trust and awareness in vaccines, vaccination, and the health system. Examples include engaging with community leaders to raise awareness about the importance of vaccination or ensuring a system for clear communication regarding potential adverse events following immunisation.



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Founded in 1962 by the Association of the British Pharmaceutical Society, the Office of Health Economics (OHE) is not only the world's oldest health economics research group, but also one of the most prestigious and influential.

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Our mission is to guide and inform the healthcare industry through today's era of unprecedented change and evolution. We are dedicated to helping policy makers and the pharmaceutical industry make better decisions that ultimately benefit patients, the industry and society as a whole.

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- Evaluation of health care policy
- The economics of health care systems
- Health technology assessment (HTA) methodology and approaches
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- Pricing and reimbursement for biologics and pharmaceuticals, including value-based pricing, risk sharing and biosimilars market competition
- The costs of treating, or failing to treat, specific diseases and conditions
- Drivers of, and incentives for, the uptake of pharmaceuticals and prescription medicines
- Competition and incentives for improving the quality and efficiency of health care
- Incentives, disincentives, regulation and the costs of R&D for pharmaceuticals and innovation in medicine
- Capturing preferences using patient-reported outcomes measures (PROMs) and time trade-off (TTO) methodology
- Roles of the private and charity sectors in health care and research
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