VACCINEINSIGHTS

RAW MATERIALS & SUPPLY CHAIN

SPOTLIGHT

COMMENTARY

Vaccine supply chains: priority areas of action emerging from the COVID-19 pandemic

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Vaccine supply chains – from raw material sourcing and production to getting vaccines into people's arms – have been widely acknowledged as a key constraint to achieving high coverage for COVID-19 vaccines globally. While there has been extensive discussion on vaccine production and access, equally important are the complexities of sourcing critical components and raw materials; installing and maintaining cold chain infrastructure; vaccine supply chain information systems; and well-trained and motivated staff to run and manage the logistics of vaccine distribution. There is an urgent need for a blueprint (and accompanying governance structure) that lays out specific technical activities, public and private investments, and coordination tasks needed for the overall vaccine supply chain to be ready to handle large demand surges such as during pandemics and large outbreaks.

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Producing vaccines and getting them into people's arms requires a carefully orchestrated global supply chain that starts with vaccine raw materials and ends with trained healthcare workers administering the vaccine to willing recipients [1,2]. Successful planning and execution of logistics can be the difference between the success and failure of vaccination campaigns. To be ready for infectious disease outbreaks and to improve coverage of routine childhood vaccination, we must make vaccine supply chains across all countries as robust as possible. While supply chains for all health products are complex [3], vaccines have the added complexity of more geographically concentrated manufacturing; many inputs/

raw materials needed for vaccine manufacturing; the need for cold chain infrastructure; guaranteeing synchronous availability of auxiliary material/immunization supplies such as vaccine-specific syringes; special immunization-related information systems; and the coordination of local, national and international vaccine shipments [4]. When vaccine supply chains don't work well, it can lead to stockouts of vaccine vials and immunization-related supplies, which can reduce vaccine coverage [5] and increase vaccination program costs due to wastage or expedited deliveries. Considerable investments and efforts have been made to improve supply chains for routine childhood immunization across countries. However, the immunization supply chain is not ready to cope with significant demand surges such as those observed in the first wave of population-wide COVID-19 vaccination. To provide a comparison, the number of COVID-19 vaccine doses distributed in the 92 low- to middle-income countries (LMICs) was two to three times UNICEF's annual supply of vaccines to LMICs. In addition, the routine immunization supply chain is largely geared towards childhood vaccination and does not have an apparatus designed for large-scale adult vaccination. Vaccine supply chains face numerous challenges, and their importance has been recognized in recent literature [4,6–8]. Similarly, the benefits of expanded regional manufacturing to improve access, and the need for greater investment in building such capabilities, have also been covered in recent literature [9,10].

To ensure vaccine supply chains worldwide are better prepared for large demand surges arising from pandemics, disease eradication efforts, or large disease outbreaks, we highlight five specific areas for concrete action (in addition to expanded regional manufacturing).

ADEQUATE CONSIDERATION OF SUPPLY CHAIN & LOGISTICS DURING VACCINE DEVELOPMENT

Global logistical constraints around cold chain infrastructure, dosing schedule, and type of syringe/delivery device are important factors that must be taken into account when developing vaccines.

Pfizer/BioNTech's mRNA vaccine, for instance, had a 0.3 mL dose in contrast with the more commonly used vaccine dosing of 0.5 mL, which required procuring specialized non-standard syringes in countries where injection safety mandates the use of auto-disable syringes [1]. As a result, 0.3 mL auto-disable syringes were in extremely short supply and presented procurement challenges for many countries. Admittedly, the tradeoff between speed of vaccine development, vaccine efficacy, and ease of supply chain/delivery is extremely complex. However, considerations such as thermostability, dose volume, number of doses, and type of syringe/device for administration should be given prominence in pre-pandemic R&D programs. Research into platform approaches to increase vaccine thermostability should be encouraged through large grant programs from R&D funding agencies globally. The development of varied vaccine delivery methods, including needle-free administration, which may be preferred by some vaccine recipients, may also create a more diversified supplier base and more diversity in terms of the syringe market's raw material needs.

At the same time, agencies responsible for decisions regarding vaccine suitability for LMICs should view thermostability in a dynamic decision-making framework and acknowledge that as more information becomes available, thermostability capabilities may improve. Hence, access to some vaccines for LMIC populations should not be completely ruled out on the basis of initial thermostability and cold-chain distribution infrastructure considerations alone.

STABLE & DIVERSIFIED SUPPLY OF RAW MATERIALS & COMPONENTS

It takes more than developing the right biological construct, plant, and equipment to produce vaccines on an industrial scale.

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Modern vaccines typically require about 9000 different materials obtained from approximately 300 suppliers in some 30 different countries [1,11]. Additionally, vaccine manufacturers need to procure more than 100 different critical components, including glass vials, culture media, filters of all kinds, tubing, stabilizing agents, resins, and disposable bags [12]. Supply problems with any one of these components or input materials can halt production of a vaccine entirely [2]. While this is a challenge for all vaccine manufacturers, it becomes particularly pronounced for new manufacturers who do not have existing long-term relationships with suppliers of such materials. COVAX and its partners led by CEPI have developed a marketplace to match suppliers of critical inputs with vaccine manufacturers who urgently need them [13]. However, some manufacturers have expressed their dissatisfaction with the ability of this marketplace to solve their sourcing problems [14]. The governance structure, technical capabilities, and partnership modalities of such a marketplace need to be carefully configured [15] and adequately resourced to solve the material sourcing problem for new and existing manufacturers, especially during a period of high demand and constrained supply. Careful consideration should be given to ensuring that such a marketplace can be maintained during inter-pandemic periods and that trade barriers do not stymie its usefulness during pandemics and large health emergencies.

COLD-CHAIN INVESTMENTS AS A LONG-TERM HEALTH SYSTEM INVESTMENT

Limitations in existing cold chain infrastructure were one of the biggest challenges for COVID-19 vaccine access and distribution. Limited cold chain capacity has long been recognized as a bottleneck in the vaccine supply chain [2]. The Cold Chain Equipment Optimization Platform (CCEOP) was set up by GAVI in 2015 to upgrade/install high-performance cold chain equipment (CCE) across LMICs, and to shape the CCE market for LMICs [16]. It financed solar direct drive and off-electrical-grid refrigerators and freezers in several GAVI-eligible countries. CCEOP explicitly took into account the fact that cold chain capacity building in LMICs is not merely about installing fridges, and freezers. It also requires building an eco-system for preventive maintenance and repair of such equipment. However, CCEOP was geared mostly towards CCE for 2–8°C – the most used temperature range across vaccines in LMICs. mRNA vaccines for COVID-19 required ultra-cold chain storage for which much of this infrastructure was not suitable. COVAX was initially focused on expanding the normal 2–8°C cold chain capacity with the assumption that much of the early supply of vaccines to COVAX countries would be 2–8°C (based on the portfolio of vaccines that COVAX had contracted). With the large-scale donations of Pfizer/BioNTech vaccines to COVAX, much of the cold chain capacity at the national and regional level had to be readied for ultra-cold chain. While some such ultra-cold chain freezers are now in place as a result of these efforts, there is a need to redesign CCEOP and its market-shaping effort around two scenarios: a) future vaccines will have better thermostability, or b) future vaccines (and other medical countermeasures) will require ultra-cold chain capacity. The redesign of CCEOP should explicitly account for the fact that cold chain investments can help in preparing the health system not just for vaccines, but for other health products such as insulin, oxytocin, and new human immunodeficiency virus treatments.

The cold chain storage capacity required in a country also depends on the configuration of the in-country vaccine supply chain. Typically, vaccines are first transported from the airport of entry to the main national distribution center from where they go to regional and district distribution centers, and eventually to immunization service delivery points. Changing this configuration e.g., distributing more directly from national distribution centers to district or health clinics, or delivering more frequently between each stage, changes the total requirement of cold chain capacity and its location [17] and may be more cost-effective and efficient. The lack of ultra-cold chain equipment at the subnational levels led to a more direct distribution system for some COVID vaccines. This more direct distribution model should be explored as a permanent option for routine vaccines. Besides improving efficiency and reducing cold chain requirements [17], this would enhance operational readiness for fast response distribution during disease outbreaks or pandemics.

COVID-19 vaccine distribution in many countries also relied on special arrangements for shipment preclearance, airspace clearance, advance documentation sharing, and sharing assets across public and private agencies. There should be an assessment of whether the ad-hoc measures for the distribution of COVID-19 vaccine can be made more systematic. Overall, there is a need for a Project-Optimize [18]-type technical task force to focus on in-country vaccine supply chain redesign in light of many new developments and provide high-level inputs to the evolving global architecture for pandemic preparedness.

IMMUNIZATION SUPPLY CHAIN DATA SYSTEMS, DEMAND FORECASTING & TRACKING VACCINE WASTAGE

A robust system that provides real-time information about vaccine stock and temperature/conditions of storage throughout the supply chain is essential to the effective and efficient distribution of vaccines, both for routine immunization [20] and particularly during a pandemic. Such visibility not only improves supply chain performance but also has the potential to help identify locations with low vaccine uptake rates and dynamically allocate stock in ways that are best suited for the public health response when supplies are scarce [19]. In many instances, the core information system that was in place for vaccine stock, flow, consumption, and temperature monitoring was expanded to include vaccination registration and scheduling. A prominent example is India's COVID-19 Vaccine Intelligence Network (Co-WIN), which was developed as an extension of the existing electronic Vaccine supply chain Intelligence Network (eVIN) [26].

Systematic collection of immunization supply chain data in real-time also facilitates better demand forecasting [20]. Analytics around uptake at sufficiently high levels of granularity, allow an understanding of drivers of vaccine hesitancy, supply availability, and other health system factor that affect demand.

COVID-19 vaccine wastage rates of up to 30% have been reported in low-income, middle-income, and high-income countries [21]. Mature supply chain stock tracking systems can also provide granular data on COVID-19 vaccine wastage, which can help identify key drivers of wastage and help develop specific interventions to minimize such wastage [21]. These interventions could include assessing the stock of vaccines globally and distributing unused vaccines to areas in need.

INVESTING IN THE PEOPLE WHO MANUFACTURE & DELIVER

In order to manufacture vaccines at scale, new vaccine plants need highly skilled staff in the areas of Chemistry, Manufacturing, and Controls (CMC), lab chemistry and analytical methods, regulatory processes, sourcing, and market dynamics [22–24]. In the period of a pandemic, the shortage of trained biomanufacturing staff can constrain vaccine production not only in new vaccine manufacturing regions, but even in established biomanufacturing clusters [12,23].

Aside from the biomanufacturing workforce, vaccine distribution requires logisticians, supply chain managers, data system managers, warehouse, and transport staff at the national, district, and health facility levels [25]. While these staff cadres exist, in many instances weak organizational systems, processes, and working environments result in staff positions not being filled. Such positions require not only technical skills but also 'social-creative' skills to solve unique problems when they arise.

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Some of the supply chain skill sets that are in short supply in public sector vaccine supply chains exist in private companies with significant supply chain footprints in the countries concerned. Platforms such as the Africa Resource Center (ARC) for supply chain management can be utilized to bring supply chain human resource capacity in the private sector to meet short-term staffing gaps in the vaccine supply chain.

In both the manufacturing and distribution areas of vaccine supply chains, it is necessary to bring together university curricula with practical internships and professional development opportunities for in-service staff. A number of initiatives are underway to address this issue, but the most important need is to establish a global network of different types of training and capability-building providers who have, or are willing to establish, an on-the-ground presence across LMICs.

CONCLUSION

The lessons learned from the COVID-19 pandemic provide a very clear set of priority actions to improve vaccine supply chains:

- The importance of considering logistics and supply chain early in the vaccine development process;
- Creating a better system for sourcing critical input materials;
- Investing in cold chain and data systems;
- Building human capital for biomanufacturing and supply chain.

The implementation of these actions will require national and global leadership, clear collaboration and coordination structures, and investment of financial resources according to needs that will vary in different settings. The new financial intermediary fund for pandemic prevention, preparedness, and response hosted by the World Bank, with technical leadership from WHO, should prioritize these action items in its financing to LMICs. Besides providing domestic financing for strengthening the vaccine supply chain, LMIC country governments should provide much-needed high-level ministerial attention to strengthening in-country vaccine supply chains.

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