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Conference report

Vaccines: New challenges, new paradigms, new opportunities: Report of the 22nd DCVMN Annual General Meeting

Rajinder Kumar Suri [a], Benoit Hayman [b,*], Sai D. Prasad [c], Morena Makhoana [d], Patrick Tippoo [d]

[a] DCVMN International, Switzerland
[b] DCVMN International, Route de Crassier 7, 1262 Eysins-Nyon, Switzerland
[c] Bharat Biotech International Ltd., India
[d] The Biovac Institute, South Africa

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ABSTRACT

The Developing Countries Vaccine Manufacturers Network held its 22nd Annual General Meeting in October 2021. Vaccine manufacturing experts, leaders from global public health organizations and dignitaries from governments and multilateral organizations discussed the challenges and opportunities emerging from the COVID-19 pandemic. Over 350 delegates from 33 countries, representing over 70 organizations partook in the meetings deliberations.

The development and scaled-up production of several safe and effective vaccines against COVID-19 resulted in over 12 billion doses being produced by the end of 2021. Unfortunately, this scientific achievement and outstanding industry effort has been overshadowed by the striking inequity in access to COVID-19 vaccines. High and upper middle-income countries have received 75% of the vaccines, while in Africa, less than 5% of the people are fully vaccinated. The inequitable access to vaccines is an issue of national health security, which has stressed the need to establish local vaccine manufacturing capacity in Africa. Key partnerships, initiatives and the deliberate strategies required to achieve sustainable manufacturing on the continent were discussed. The ability to acquire technology, access markets and financing mechanisms, and workforce development were reported as key enablers to achieving a healthy ecosystem.

Innovative vaccine technologies, new regulatory approaches, and the importance of voluntary technology transfers in increasing the global supply capacity of both COVID-19 vaccines and traditional vaccines were highlighted. In reviewing the lessons learned from the pandemic, speakers shared a consensus that innovation and partnerships will be central to any solution proposed to mitigate the current pandemic and prepare for future ones.

1. Introduction

The Developing Countries Vaccine Manufacturers Network (DCVMN) hosted its 22nd Annual General Meeting (AGM) from the 19th to 21st October 2021. The virtual meeting, co-hosted by Biovac of South Africa, gathered over 350 experts and leaders from industry, research institutes, global health organizations, and multilateral organizations. Key topics included the inequitable access to COVID-19 vaccines, sustainable manufacturing, and innovative vaccine technologies and financing mechanisms.

The inaugural address was delivered by H.E. Dr. BE Nzimande, MP, Minister of Higher Education, Science and Innovation of South Africa. Dr. Nzimande, while thanking the dignitaries and the organizers, stressed that the COVID-19 pandemic has not only caused the death of millions of people around the world, but has also destroyed livelihoods.

Sharing the vision of H.E. Cyril Ramaphosa, Honorable President of South Africa, Dr. Nzimande highlighted the urgent need to address vaccine inequity and to expand vaccine manufacturing capabilities in Africa, stating that one of the biggest challenges of the current pandemic is that those in the developing world are still largely waiting for vaccines. He concluded that active collaboration and fostering partnerships will be crucial in ending the COVID-19 pandemic and building the capacity to deal with future pandemics.

2. Vaccines: new challenges, new paradigms, new opportunities

Dr. Tedros A. Ghebreyesus (WHO), in his keynote address, stated:

* Corresponding author.
E-mail address: b.hayman@dcvmn.net (B. Hayman).

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"The development of not one, but several safe and effective vaccines against COVID-19 in record time is a triumph for science, but the shocking inequity in access to those vaccines is a failure for humanity. Know-how, technology, licenses, and intellectual property remain in the hands of a few, leaving millions of people at risk".

He asserted that WHO continues to work with their partners to explore all avenues to rapidly scale-up production in low- and middle-income countries (LMICs), including technology transfer, voluntary licensing, and a waiver on intellectual property (IP) rights. In stressing the need for increased investment in local production capacity in all regions, he mentioned that DCVMN is more important than ever.

Reporting on the Access to COVID-19 Tools Accelerator (ACT-A) at 18 months, Dr. Bruce Aylward (WHO) reminded the audience that the ACT-A was launched to accelerate the development of tests, treatments, and vaccines for COVID-19. He commended the industry for creating and scaling these tools, particularly the scientific advancements in the area of vaccines. Importantly, the ACT-A has also put mechanisms in place to ensure the equitable uptake and use of these tools (Fig. 1). If the inequities are not solved, it is estimated that at least 5 million additional lives will be lost in 2022 and 5.3 trillion would be lost in economic output by 2026 [1].

The third keynote address was delivered by Dr. Seth Berkley (Gavi). Between 2016 and 2020 Gavi helped countries immunize 324 million unique children and avert 6.9 million future deaths [2]. Dr. Berkley noted that this was only possible thanks to a supplier base that has evolved from five suppliers, including one DCVMN member, to 18 suppliers in 2021, with more than half of them based in Africa, Asia, and Latin America. Furthermore, the investments made by developing country vaccine manufacturers (DCVMs) in research and development (R&D), production capabilities and quality assurance have been critical to ensuring that the supply of high-quality, affordable vaccines meets the growing demand [3,4].

Dr. Richard Hatchett (Coalition for Epidemic Preparedness Innovations, CEPI) stated that from CEPI's vantage point there are six major positives emerging from the pandemic. First and foremost, the advances in technology: new vaccine platforms, new approaches to the use of mRNA, innovations in manufacturing, and the revolution in the underlying vaccinology. Second, are the cumulative innovations across many different vaccine programs and different regulators that helped speed vaccines through clinical development, manufacturing scale-up, and regulatory processes. Third are the new concepts of preparedness that have been validated during the pandemic. Fourth are the new institu-

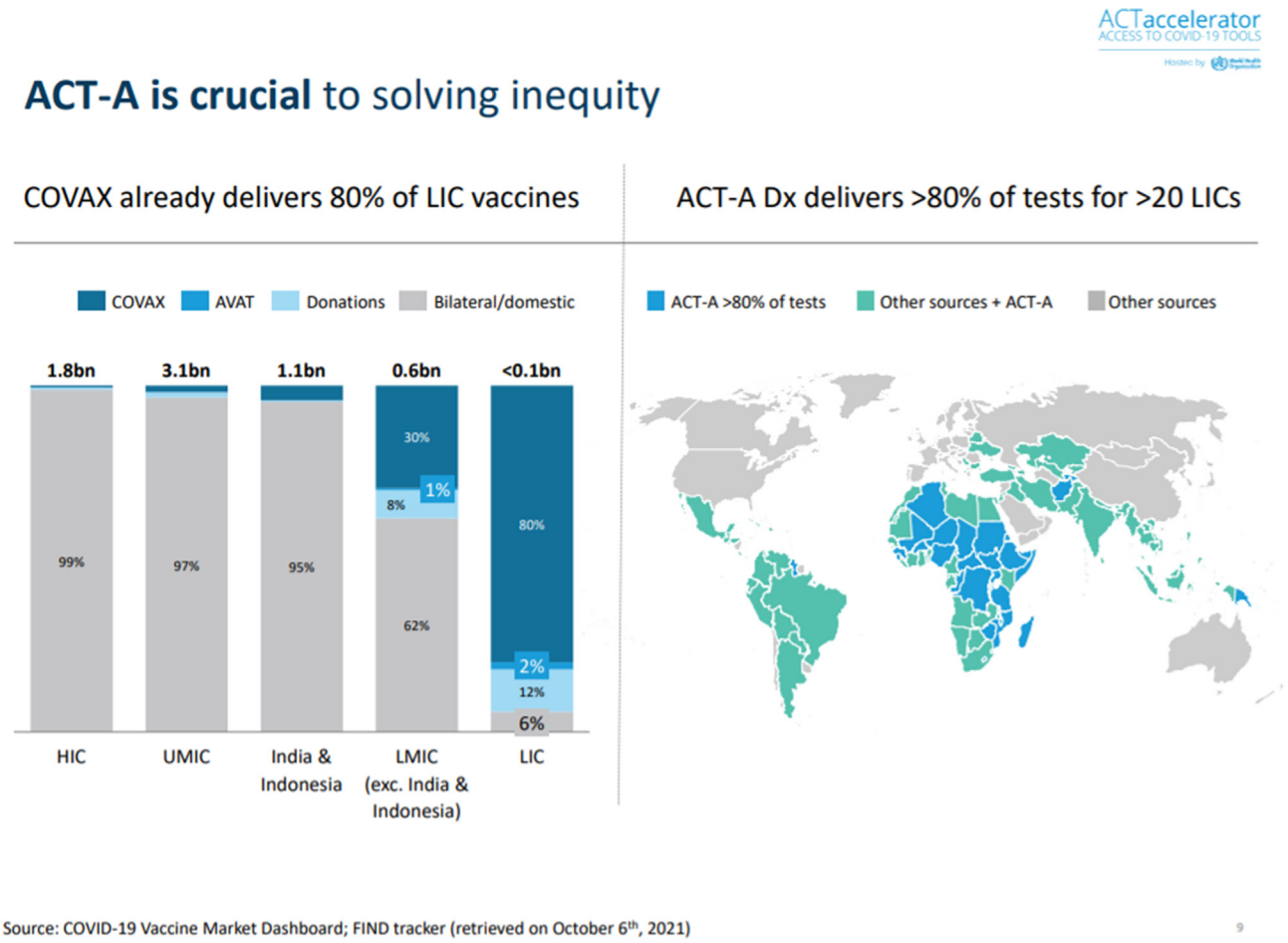

Fig. 1. Graphical representation of the ACT-A efforts in supporting equitable access to COVID-19 tools. The COVAX Facility, the vaccines pillar of the Access to COVID-19 Tools (ACT) Accelerator, is critical to solving the problem of inequitable access to COVID-19 vaccines. 80% of vaccines delivered to lower income countries (LICs) have been delivered through the COVAX Facility. 30% of vaccines to low- and middle-income countries (LMICs), excluding India and Indonesia, which have strong domestic production, are delivered through the COVAX Facility. To supply COVAX and address inequities the cooperation with vaccine manufacturers is essential. Additionally, the ACT Accelerator has delivered over 80% of the COVID-19 tests to more than 20 LICs. Figure reflects data retrieved on the 6th October 2021. Source: COVID-19 Vaccine Market Dashboard. https://www.unicef.org/supply/covid-19-vaccine-market-dashboard FIND SARS-COV-2 Test Tracker. https://www.finddx.org/covid-19/test-tracker/ (Courtesy of B. Aylward).

tional arrangements and multi-sectoral partnerships represented by efforts such as the ACT-Accelerator, COVAX, and the emerging partnership between WHO, the International Monetary Fund (IMF), the World Bank, and the World Trade Organization (WTO) [5]. Fifth is the emergence of new regional mutual security partnerships, and finally, there is a moment of unprecedented political will to address the threat of epidemic and pandemic disease with the seriousness warranted.

Quoting Rahm Emanuel in saying "You should never let a serious crisis go to waste", Dr. David C. Kaslow (PATH) mentioned that this could not be any truer for DCVMN and its members as the pandemic heads towards a third year. He stated that the COVID-19 pandemic has widened rather than narrowed the preexisting immunization gap between high income countries (HICs) and LMICs [6]. Differences in immunization are not solely attributed to the supply and affordability of vaccines, but also to the cost to healthcare systems in low-income countries to deliver vaccines [6]. Furthermore, Dr. Kaslow discussed the topic of vaccines as public goods, noting that in 2020, the UN General Assembly adopted a resolution recognizing immunization against COVID-19 as a global public good [7]. He highlighted that the manufacturing and procurement of private goods, the means by which vaccines are currently marketed, is strikingly different to how public goods and services are manufactured and procured.

Speaking to the demand and supply of vaccines in LMICs, Dr. Derrick Sim (Gavi) stated that vaccines are one of the best investments for governments to promote strong health, social, and economic benefits. Gavi, and their partners currently support vaccines against 17 infectious diseases. By the end of 2019, Gavi had supported close to 500 routine introductions and campaigns, and funded stockpiles of more than 135 vaccines [8]. He reported that, during the COVID-19 pandemic, DCVMN manufacturers are not only supporting the production of vaccines, but accelerating technology transfers, which will have a mid- to long-term impact on their innovative capabilities and the supply landscape of wider vaccines in the future.

Dr. Soumya Swaminathan (WHO) discussed priorities in global public health. She stated that the lessons learned from the international effort to develop and produce COVID-19 vaccines must be carried over to existing infectious diseases, such as tuberculosis (TB). Additionally, new platforms and technologies used in response to the COVID-19 pandemic can provide benefits beyond infectious diseases; for example, the application of mRNA to develop cancer vaccines [9].

Dr. Solomon Zewdu (Bill & Melinda Gates Foundation, BMGF) reported on the Foundation's role in mitigating global COVID-19 challenges. He commented that developing countries, but more specifically, the African continent is no stranger to vaccine manufacturing, rather it is a stranger to the sustainable ecosystem that effectively manufactures vaccines to meet the continent's needs. The Gates Foundation have been supporting the building blocks of a sustainable and effective ecosystem that assures the success of existing manufacturing facilities and any additional ones that organically form in the future. Efforts are focused on reducing barriers to enable DCVMs to meet global vaccine demand now and in the future.

Dr. Rogerio Gaspar (WHO) addressed the topic of the Collaborative Registration Procedure (CRP): A win–win situation for National Regulatory Authorities (NRAs) in LMICs, manufacturers and WHO. He emphasized the reliance on the regulatory system, saying "Reliance has been at the center of this crisis. Reliance helps to transfer the regulatory information from trusted sources, facilitating country approval." The World Health Assembly (WHA) recognizes that inefficient regulatory systems can be a barrier to access to safe, effective, and quality medical products [10]. The goal is to get pre-qualified approved products to patients faster and more efficiently, as well as ensuring continued supply of quality assured products post-registration.

3. Innovations in vaccine space

Dr. Carissa Etienne (PAHO) reported that the Americas have been the epicenter of the pandemic, with more than two million deaths. Citing several examples over the last decade where the region has been affected by epidemics of cholera, dengue, yellow fever, chikungunya, Zika, and the 2009 H1N1 pandemic of influenza, she said "Our region is very well practiced in dealing with epidemics". To strengthen regional health systems, PAHO has implemented a Safe Hospitals and Smart Hospitals initiative. In a joint effort with countries and territories in the Americas this has contributed to ensuring that hundreds of healthcare facilities remain accessible and functional at maximum capacity, during disasters or epidemics [11].

Aurelia Nguyen (Gavi) reported that the COVAX Facility and their partners have met or exceeded several key targets, mostly related to fundraising and securing vaccines. She added that the COVAX Facility, however, can only be successful if deals and money raised translates into shots in arms. Supply disruptions due to delays in the development and approval of vaccines, export bans, and other factors, have caused difficulties for the COVAX Facility to deliver two billion doses in 2021. Ms. Nguyen elaborated on mitigation plans including dose sharing and the efforts of the COVAX Manufacturing Task Force.

Dr. John Nkengasong (Africa CDC) remarked that access to vaccines is truly a security issue. A key lesson from the COVID-19 pandemic is that global health security starts at the national level, and national health security depends on regional health security. On April 12–13, 2021, the Africa CDC hosted a summit which gathered 40,000 people to discuss the critical need for vaccine manufacturing in Africa. Dr. Nkengasong stated that a coordinated approach to define the ecosystem for vaccine manufacturing and develop a framework is needed as Africa moves from importing 99% of vaccines to manufacturing about 60% of their vaccines in the next 20 years [12].

Thomas Cueni (International Federation of Pharmaceutical Manufacturers and Associations, IFPMA) speaking on the success story of the vaccine industry, commented that the unprecedented development at record speed would not have been possible if everybody had done business as usual. Mr. Cueni highlighted the setbacks in terms of scaling up manufacturing, in addition to export restrictions that led to shortages of raw materials and supply chain problems. In face of these setbacks, he commended the efforts of manufacturers from developing countries and industrialized countries in scaling up global vaccine capacity. It is estimated that by the end of 2021, 12 billion COVID-19 vaccines will have been manufactured, indicating the global vaccine capacity has more than tripled since pre-pandemic [13].

Dr. Mariangela Batista Galvao Simao (WHO) stated that the large number of doses produced hid a massive inequity. High and upper middle-income countries have received 75% of the vaccines, while in continents, like Africa, less than 5% of the people are fully vaccinated. She declared this fact self-defeating because we cannot end this pandemic by over vaccinating certain populations, while under vaccinating many more. To achieve the WHO global target of vaccinating 40% of the population in every country by the end of 2021 and 70% by the middle of 2022, the challenge is no longer supply but equitable distribution [14].

Dr. Michelle McMurry-Heath (Biotechnology Innovation Organization, BIO) affirmed that innovation by biotech companies will continue to be vital as we control the pandemic and future ones. She highlighted industry partnerships that have paired ample

resources with unique research and technologies. Dr. McMurry-Heath noted several lessons learned from the COVID-19 pandemic. A strong innovation ecosystem to empower innovators by protecting IP and R&D incentives is critical. Early-stage investments taking emerging ideas to products, investments in sustainable manufacturing globally, and forging more development and manufacturing partnerships are all key as we move forward.

Dr. Jerome Kim (International Vaccine Institute, IVI) made the point that a failure of equity had three predictable consequences. The first was a humanitarian crisis. COVID-19 deaths are greater than predicted from the failure to provide vaccines to populations equally [15]. Secondly, without equity, 50% of the global economic cost of the pandemic in 2021 would be borne by advanced economies [16]. Lastly, vaccine inequity has biological consequences. Failure to control the pandemic, to use the vaccine systematically in populations, will generate mutants that may undermine the efficacy of the current vaccines and that of vaccines in the future.

Prof. William Kwabena Ampofo (African Vaccine Manufacturing Initiative, AVMI) presented AVMI's mission to promote the establishment of vaccine manufacturing in Africa. The AVMI aims to ensure that Africa has the capacity to manufacture vaccines, to break the cycle of dependency that the COVID-19 pandemic made evident. He reported that AVMI is working with various partners looking at access to infrastructure, appropriate technology, the funding and financing requirements, the market dynamics, and the manpower skills that will be required to establish sustainable vaccine manufacturing in Africa.

4. CEO Forum: Vision 2030

Joshua Chu (Clinton Health Access Initiative, CHAI), moderating a panel discussion on the vision for 2030, asked industry leaders to share their vision for their respective organizations.

Jaeyong Ahn (SK bioscience) reported that with increasing demand for vaccines, SK bioscience is expanding its manufacturing facilities to triple their current level of 500 million doses in the next three years. Furthermore, SK bioscience is strengthening their R&D capabilities by acquiring new technology platforms and recruiting global talent. SK bioscience has the vision to expand their product portfolio and enter new markets.

Dr. Andrew Wong (Walvax) shared Walvax's aspiration to become a vaccine manufacturer with global reach. Walvax has seven vaccines in their product pipeline, including a mRNA COVID-19 candidate currently undergoing Phase III trials in Mexico and Indonesia. Furthermore, with support from CEPI and BMGF, Walvax has an adenovirus-based protein subunit COVID-19 candidate in Phase II clinical development in China.

Dr. Mauricio Zuma (Bio-Manguinhos/Fiocruz) stated that acquiring the technology transfer of the Oxford/AstraZeneca vaccine and scaling up production was challenging but was achieved in a few months. To date, Bio-Manguinhos/Fiocruz has produced more than 110 million doses. Bio-Manguinhos/Fiocruz is also focused on developing their own vaccine and have a mRNA COVID-19 vaccine candidate in preclinical development. With WHO support to accelerate development, this vaccine will be shared with other countries in the Latin American region.

Dr. Alejandro Gil (Sinergium Biotech) shared that Sinergium was founded in 2009 during the flu pandemic. Since then, Sinergium has engaged in more than seven technology transfers and, through continued investments and partnerships, expanded their capabilities and the capacities of their facilities. Dr. Gil highlighted the importance of sharing new technologies to enable faster vaccine supply and affordable prices for both COVID-19 vaccines and vaccines in the national immunization schedule.

Dr. Morena Makhoana (Biovac) stated that in 2019, pre-pandemic, Biovac's 2030 strategy was to diversify their use of technology platforms and increase vaccine supply to markets beyond South Africa. He reported that changes caused by the pandemic have not only validated their initial strategy but have also launched opportunities such as Biovac's engagement in the WHO mRNA hub in South Africa [17].

Responding to a question on over-capacity, Mr. Chu summarized the panelists' responses, stating "In light of the current shortages, we should not be afraid of oversupply, but we should work together to ensure that supply reaches those that need it the most".

5. Challenges and opportunities in vaccine research and availability

Dr. Melanie Saville (CEPI) reported on the achievements and challenges ahead for the COVAX Manufacturing Task Force (Fig. 2A, Fig. 2B). The Task Force was established following the Global Manufacturing and Supply Chain Summit hosted by COVAX, DCVMN, BIO, and IFPMA in March 2021, which gathered global health leaders to discuss actions to optimize the production and supply of COVID-19 vaccines globally [18]. Specifically, the Task Force's objectives are to end the acute phase of the pandemic by optimizing short term vaccine manufacturing, requiring that the shortage of input supplies is met, and COVAX is prioritized to ensure that LMICs receive vaccines.

A report on Expanded Program on Immunization (EPI) vaccine distribution was provided by Etleva Kadili (UNICEF). Since the onset of the pandemic, lockdowns and flight disruptions have resulted in over 100 immunization campaigns being postponed, with many more cancelled. In 2020, the volumes of vaccine doses shipped decreased by 11% compared to the previous year [19]. Despite resources being redirected to support COVID-19 vaccination she reported that recovery activities are steadily returning the number of vaccine deliveries to pre-pandemic levels. The total number of routine vaccines delivered in Q3 2021 is roughly equal to the levels achieved in Q3 2019 [19].

Prof. Pieter Neels (Vaccine Advice BVBA) discussed how COVID-19 vaccines received Emergency Use Listing (EUL) in less than 12 months. He noted that knowledge of the virus was critical, particularly scientists' efforts in rapidly recognizing it as a SARS virus and the international collaboration in sharing data. Furthermore, the pandemic preparedness programs of regulatory agencies, in addition to high levels of funding to develop vaccines, shortened timelines. Notable, the acceptance of platform technologies, which has allowed the licensing of the technology instead of a vaccine, has been key in accelerating the timelines of the COVID-19 vaccines on the market (Fig. 3).

Dr. Kate O'Brien (WHO) outlined how supply and demand for other antigens has been impacted by the pandemic itself and the COVID-19 vaccine production and introduction. Particularly, Dr. O'Brien reported that there is a risk of a supply–demand unbalance for measles and pneumococcal conjugate vaccines. Further discussing the impact of the pandemic, she highlighted five factors that could impact mid- to long-term demand forecasting: stopping of immunization services, changes in health seeking behavior, disruption of workforce availability, inefficiencies in cold chain and logistics systems, and lastly the economic downturn. The WHO is undertaking a series of actions to mitigate the impact of COVID-19 on the markets for other antigens (Fig. 4).

Ms. Carmen Rodriguez Hernandez (WHO) provided an overview of the activities that WHO has implemented to assess COVID-19 vaccines and to facilitate regulatory approvals in countries, for which WHO asks NRAs to rely on the EUL. To facilitate expedited national approval, WHO has shared dossiers and EUL reports with

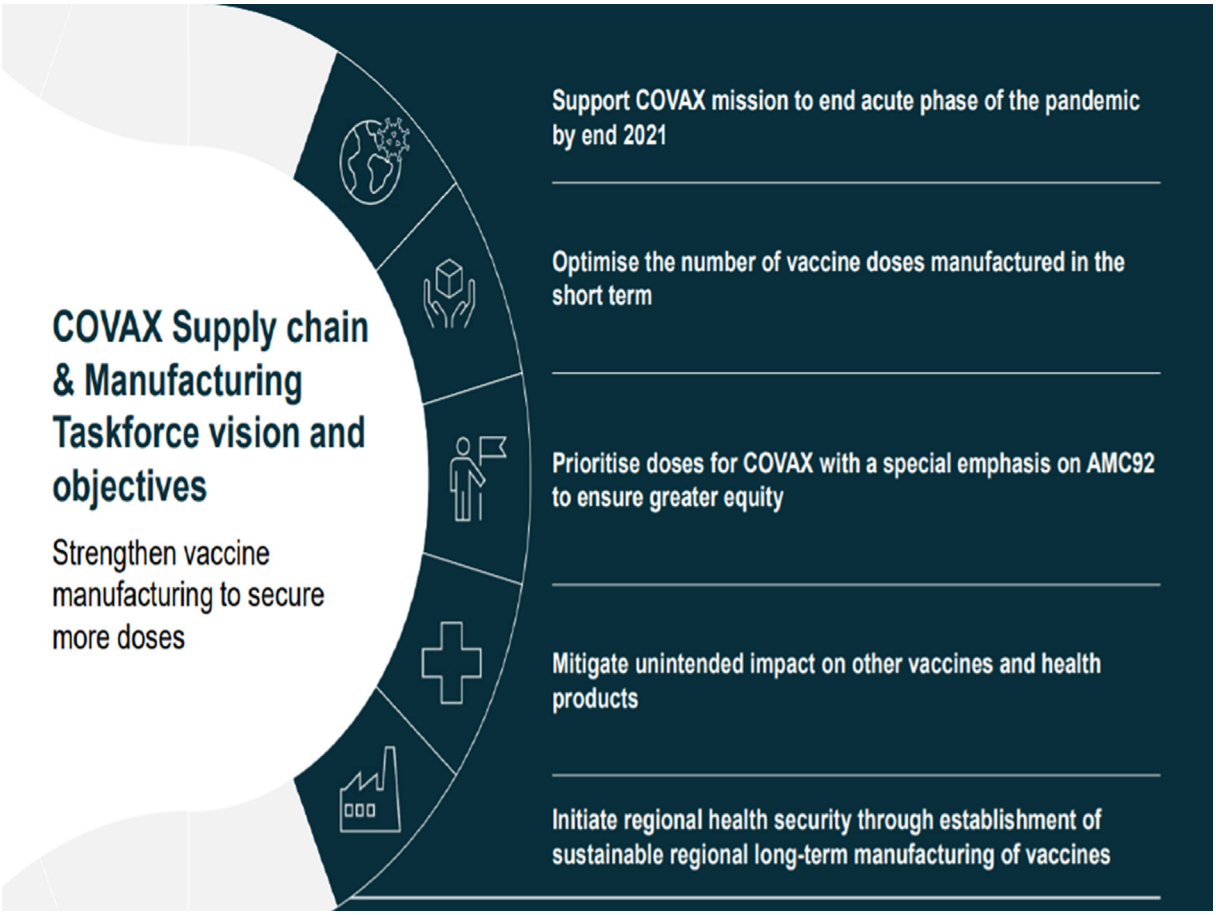

Fig. 2A. The vision and objectives of the COVAX Manufacturing Task Force. The shortage of raw materials and trade barriers have jeopardized the ability of manufacturers to produce and supply vaccines to where they are needed most. To address these issues the COVAX Manufacturing Task Force was established. The Task Force is co-led by CEPI, Gavi, WHO, and UNICEF in partnership with BMGF, IFPMA, DCVMN, and BIO. (Courtesy of M. Saville).

over 100 countries, facilitated workshops and engaged in one-on-one discussions based on the outcome of the review (Fig. 5). More than 100 countries have granted Emergency Use Authorization (EUA) within fifteen days post EUL [20].

Dr. Raman Rao (Hilleman Laboratories) discussed technology transfer strategies that are important in enabling technology platforms which play a crucial role in vaccine availability, supply, and pricing, which is particularly pertinent to LMICs. There is a new evolution in technology transfer strategies with the availability of technology transfer hubs, such as the mRNA hub in South Africa, which have the potential to improve equitable access to technologies and vaccines. Dr. Rao commented on the importance of manufacturing innovations such as modular facilities, to reduce costs and facilitate the technology transfer process.

6. Innovative financing mechanisms to ramp up manufacturing in Africa and other LMICs

Gwen Mwaba (Afreximbank) reported that at the onset of the pandemic global shortages and export bans for essential medical supplies resulted in Africa's import orders not being fulfilled. Similarly, vaccine nationalism resulted in developing countries being left behind once more. Citing this tight supply situation, the Afreximbank, alongside its partners developed the Africa Medical Supplies Platform (AMSP), a marketplace to implement the African Union's pooled procurement strategy for COVID-19 supplies. Furthermore, with the support of Afreximbank's $2 billion advanced procurement facility, the African Vaccine Acquisition Task Team successfully negotiated a procurement contract for 400 million vaccine doses for African countries [21].

Sérgio Pimenta (International Finance Corporation, IFC) announced that the World Bank are accelerating their efforts to ensure that more vaccines are produced in Africa for Africa. To safeguard health security Africa's goal is to become more self-sufficient. To help achieve this goal Mr. Pimenta reported that the World Bank is making available $12 billion for the acquisition and deployment of vaccines [22]. After elaborating on several of the IFC's initiatives on the continent, he stated that "partnerships are key to success, not only to pursue resilient recovery but to lay the foundation for stronger vaccine manufacturing development".

Prof. Robin Shattock (Imperial College London), in discussing capacity building in LMICs, highlighted the importance of partnerships to feed technological advancements into the manufacturing process. In this context he spoke about the Future Vaccine Manufacturing Research Hub, which was set up to partner on a technological basis with different manufacturers globally. The hub-spoke model brings together academia, industry, and institutions to work on shared projects, with a focus on bringing new and emerging technologies to partners around the world.

Dr. Kelvin Lee (The National Institute for Innovation in Manufacturing Biopharmaceuticals, NIIMBL) reported that in assessing workforce development needs there are common challenges faced by manufacturers in both developing and high-income countries. Namely, manufacturers have difficulty finding and retaining talent, and there is a need to provide training for emerging technologies in

Fig. 2B. Workstreams and accomplishments of the COVAX Manufacturing Task Force. The Task Force is divided into three workstreams. Workstream 1 focuses on the immediate COVAX response. Workstream 2 focused on the mid-term COVAX response. Workstream 3 is centred on long-term sustainable manufacturing. Workstream 1 launched a COVAX Marketplace in July 2021. Match-making within this marketplace led to an additional 78 million doses of COVID-19 vaccines being supplied to the COVAX Facility. (Courtesy of M. Saville).

automation, data science, virology, and for approaches to mRNA vaccine manufacturing. There are unique challenges that exist among DCVMs, however, solutions are difficult to generalize due to the differences in manufacturers and the countries they are based in. Nevertheless, Dr. Lee reported that with many organizations investing in global vaccine manufacturing workforce development, global collaboration is critical to workforce development success in developing countries.

Mr. Lin Xiangliang (ESCO Aster) reported on the essential role of Contract Development and Manufacturing Companies (CDMOs). CDMOs provide enabling technologies to scale-up manufacturing and bridge development processes. For example, technology transfer to existing manufacturing facilities or those being built in parallel to clinical trials enables rapid scale-up production. ESCO Aster has an office in South Africa to support local vaccine manufacturers and enable self-sufficiency on the African continent.

Jon Pearman (Temptime, a Zebra company) provided an update on vaccine vial monitors (VVMs). The increase in shipments of COVID-19 vaccines into Africa, plus the use of multiple vaccines with different requirements will bring complexity to the supply chain and healthcare workers. VVMs confirm cold chain storage conditions have been appropriately maintained, helping vaccine handling and administration. This is particularly important when considering the re-distribution of COVID-19 vaccines within and between LMICs. The WHO Target Product Profiles (TPP) for COVID-19 vaccines have VVMs as a preferred characteristic under EUL [23].

7. Priorities & policies for LMICs – a multilateral view

Regulatory challenges in adopting new technologies in LMICs were discussed by Prof. Gagandeep Kang (Christian Medical College Vellore). A key question being discussed by regulators is whether countries with low coverage in Africa will permit placebo-controlled trials to fast-track clinical testing. She also discussed scenarios in the absence of placebo-controlled trials, which will not be permitted by regulators in most parts of the world, with immuno-bridging being the most discussed among regulators and the most likely approach.

The global roadmap for research and development of tuberculosis vaccines [24] was discussed by Prof. Frank Cobelens (Amsterdam University Medical Centers). He stated that WHO has set a target to reduce the incidence of tuberculosis by 2035 by 90%, but that is very unlikely to be achieved without a more effective vaccine. The critical unmet global public health need prompted the development of a global roadmap which examines barriers to vaccine R&D (Table 1).

Prof. Tulio de Oliveria (University of Kwazulu-Natal) reported on SARS-COV-2 genomic surveillance. He discussed the recently

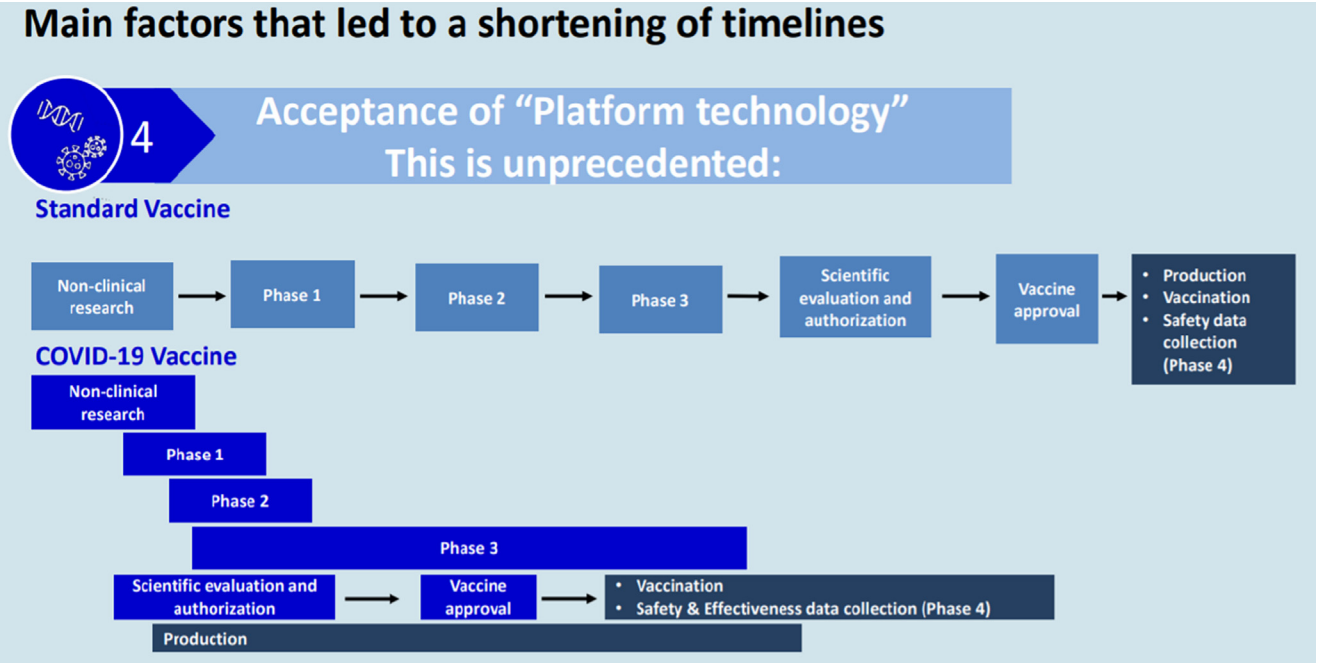

Fig. 3. Accelerating COVID-19 vaccine development. Development timelines can be reduced by conducting non-clinical research in parallel to phase I clinical studies; hence phase II trials can commence more rapidly. Source: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-development-evaluation-approval-monitoring (Accessed 23 February 2022). (Courtesy of P. Neels).

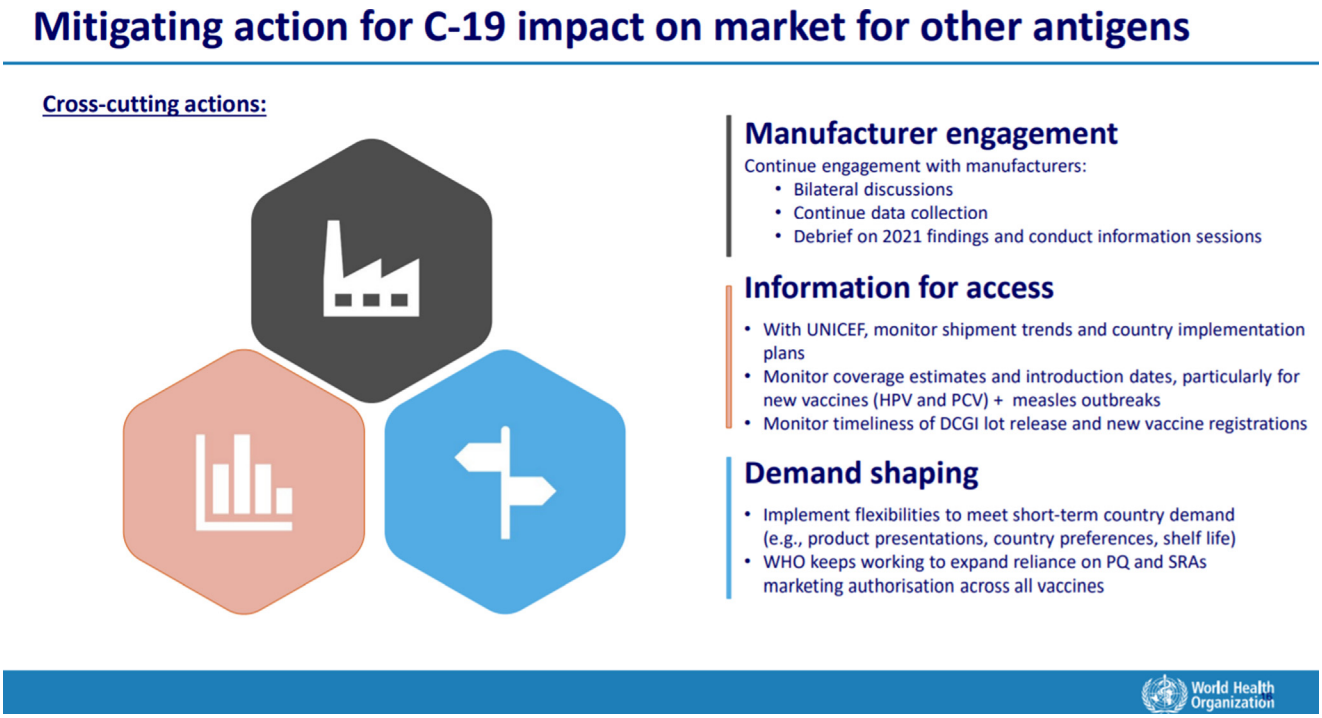

Fig. 4. Mitigation action for COVID-19 impact on market for other antigens. WHO has implemented a series of cross-cutting actions centred on manufacturer engagement, information for access and demand shaping to address the downturn in routine immunization caused by the COVID-19 pandemic. (Courtesy of K. O'Brien).

created Center for Epidemic Response and Innovation (CERI), which has set up a network of genomics labs in South Africa. Genomic surveillance has enabled the real-time identification of variants of concern [25]. Once the Beta variant was identified as a variant of concern, the virus was grown in the laboratory and tested against vaccines on the market over time to guide the selection of the most effective vaccines against the variant [26]. Additionally, the CERI has shared their genomic surveillance technology widely in Africa, resulting in the Pan-African Genomics Surveillance Collaboration bringing together 122 African and 25 international organizations.

Dr. Narendra K. Arora (INCLEN Trust International) discussed the important challenge of vaccine safety surveillance, a challenge compounded in resource constrained settings. Subsequently,

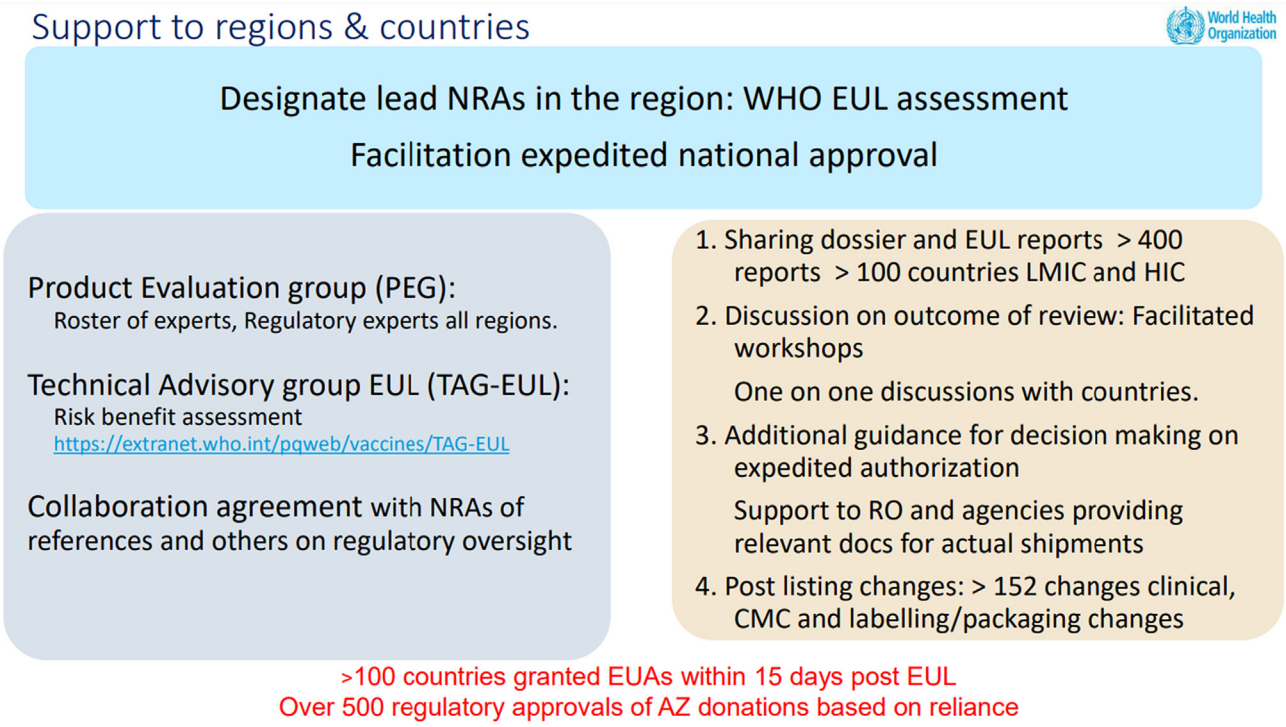

Fig. 5. WHO EUL assessment facilitates expedited national approval. The WHO Emergency Use Listing (EUL) assessment process involves a Product Evaluation Group (PEG), which is compiled of regulatory experts from all regions. The PEG assesses the quality, safety and efficacy of the COVID-19 vaccine product before the Technical Advisory Group (TAG-EUL) conducts a risk–benefit assessment and recommends the product for WHO EUL. Additionally, during this process WHO has collaboration agreements with NRAs that perform regulatory oversight. To facilitate expedited national approval, WHO has shared dossiers and EUL reports with over 100 countries, facilitated workshops, and engaged in one-on-one discussions based on the outcome of the review. (Courtesy of C. Hernandez).

Table 1
Identification of barriers to R&D for tuberculosis vaccines. The barriers to R&D for tuberculosis vaccines were grouped into four categories. In each category, key barriers were identified. The complete *Global roadmap for research and development of tuberculosis vaccines* is available at http://www.edctp.org/publication/global-road-map-for-research-and-development-of-tuberculosis-vaccines/# (Courtesy of F. Cobelens).

Category	Specific barriers
Diversifying the pipeline	• Too narrow approach in regards to antigens, platforms, and delivery
Accelerating clinical development	• Lack of validated animal models that predict efficacy in humans • Lack of validated laboratory correlates for protection • Need for large-scale phase III trials with disease endpoint
Ensuring public health impact	• Lack of clear value proposition for countries to introduce a TB vaccine • Limited insight in how a TB vaccine for adults would be used & accepted • Poor insight in global and national demand and willingness to pay
Enabling conditions	• Limited and fragmented funding • Siloed science • Limited stakeholder engagement

adverse events are not picked up with the sensitivity desired for new vaccines, particularly those based on new vaccine platforms. He added that the lack of data on vaccine safety surveillance extends approval timelines, an issue particularly affecting DCVMs. Manufacturers must collaborate with Ministries of Health to ensure post-marketing surveillance is prioritized.

Tania Cernuschi (WHO), reflecting on the vaccination progress in lower income settings over the past few decades, stated that the pandemic has triggered the need for a paradigm shift from sequential and risk-averse vaccine development to a rapid approach, compressing time to market while not compromising quality and safety. Actions to ensure sustainable access globally are listed in Table 2.

Dr. Frederik Kristensen (CEPI) discussed CEPI's roles in enabling accelerated vaccine R&D and manufacturing for emerging infectious diseases in LMICs (Fig. 6). While CEPI primarily focuses on R&D, the pandemic identified a need for CEPI to support manufacturers, and in this area, CEPI will focus especially on innovations that make manufacturing more cost effective and brings it closer to outbreaks.

Dr. Brigitte K. Giersing (WHO) presented a new WHO initiative: Evidence Considerations for Vaccine Policy (ECVP), which will offer a systematic approach to inform vaccine developers of the evidence anticipated to facilitate global policy recommendations [27]. The initiative is important because for vaccines intended to be deployed in LMICs key steps including global policy recommendation, WHO pre-qualification and financing require a different set of data and evidence requirements than what is needed for product registration. She noted that if stakeholders, who play a critical role in the development process, are not aligned, it poses a risk to manufacturers and can jeopardize investments needed to advance products to late-stage product development. It also risks causing a delay between product approval and implementation.

Dr. Jicui Dong (WHO) reported that a WHA resolution on *Strengthening local production of medicines and other health technologies to improve access* was adopted at the 74th WHA [28]. Subsequently, WHO announced a new initiative, The World Local Production Forum (WLPF). The WLPF, is a regular forum to stimulate high level dialogue and action, promote collaboration, and shape the global direction in promoting local production to improve timely, equitable access. During the first WLPF in June

Table 2
Features of a paradigm shift needed to ensure sustainable and timely access globally. (Courtesy of T. Cernuschi).

Actions to ensure sustainable and timely access to vaccine globally
Establish early, evidence-informed strategic goals and leadership that serve the collective global health interest.
Shoulder risks and invest aggressively to address the needs of today and prepare for future emergencies.
Strengthen market preparedness by investing in: • new vaccine technologies • regional research, development, and manufacturing hubs and insurance • enabling regulatory harmonization • market transparency and oversight
Define principles and operational details for collaboration in times of scarcity that enable countries to protect their own citizens while ensuring that no country is left behind.

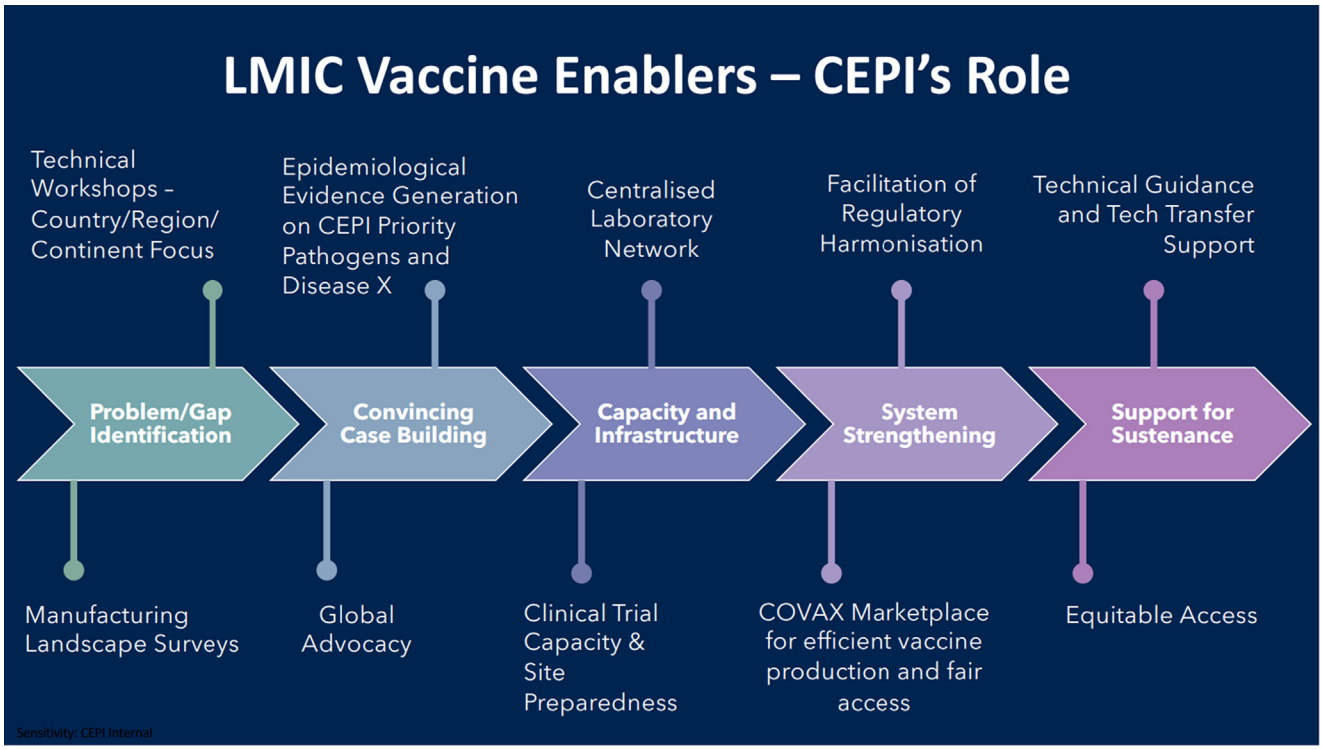

Fig. 6. Vaccine enablers in LMICs. CEPI, in coordination with partners, have several initiatives to enable vaccine R&D and manufacturing in LMICs. (Courtesy of F. Kristensen).

2021, a key session discussing building capacity to enhance access to vaccines was held (Fig. 7).

8. Facilitating manufacturing ramp-up

Josephine Cheng (Merck) discussed the evolution of the vaccine manufacturing process and how COVID-19 highlighted the need for agile manufacturing. She introduced the flexible factory, which integrates single-use technologies into digital, modular designs. This approach helps achieve process simplification and reduces equipment footprint.

A vision to build smart factories for the future was outlined by Tony Xu (Tofflon). Tofflon provides innovative solutions for drug development and manufacturing processes. Several COVID-19 vaccine projects were discussed in detail.

Dr. Vibin B. Joseph (BiOZEEN) explained the challenges in ramping up vaccine production, citing the complexities and variances in the different manufacturing processes for the different types of vaccines. The tension between cost, customization and time has led BiOZEEN to develop need-based customized solutions, with the objective to accelerate speed, reduce cost, and increase flexibility and customization.

Stephanie Krieg (Bioengineering) discussed increasing manufacturing output by leveraging existing facilities. Namely, she shared two case examples: increasing production volume of existing vessels to increase the harvest of the end product, and increasing cell density and shortening batch duration, which increases efficiency, product yields and profitability.

Dr. Andreas Castan (Cytiva) presented flexible approaches to address modern vaccine demand. Discussing challenges related to mRNA manufacturing, he noted many operations are distributed and few manufacturers are inadequately equipped to work on all parts of the process. Cytiva has worked to create optimized process workflows and provide equipment for end-to-end support for a vast number of processes.

Benefits of an integrated solution were discussed by Christian Lavarreda (Syntegon). Integrated solutions optimize plant layout, help coordinate processes, and generate cost savings through shared peripherals. These features generate key benefits including better yields with a smaller footprint, smaller capital investment, and therefore lower risk and faster project execution.

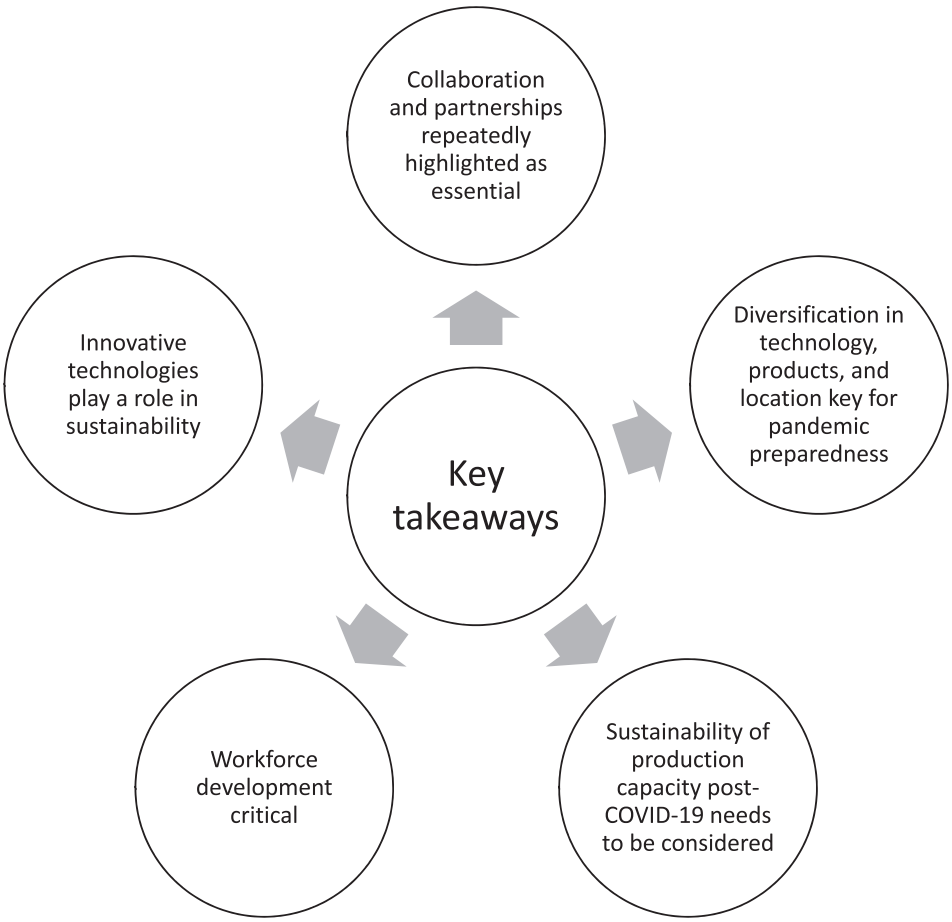

Fig. 7. Key takeaways form the discourse on building capacity to enhance access for vaccines and biologics during the first WLPF. The first World Local Production Forum (WLPF) convened in June (21–25), welcoming high-level delegates from more than 100 member states and other stakeholders in the global community. The complete meeting report is available at https://www.who.int/publications/i/item/9789240032422 (Courtesy of J. Dong).

9. Sustainable manufacturing in Africa

Samir Desai (Zydus Cadila) moderated a panel discussion on sustainable manufacturing in Africa. Dr. Matthew Downham (CEPI) discussed CEPI's work mapping vaccine manufacturing across Africa, Latin America, Caribbean, Southeast Asia, Western Pacific, and the Middle East, reporting the aspirational plans of organizations to technically diversify and expand their existing human vaccine manufacturing capacities [29]. Speaking more broadly on the topic of sustainability, Dr. Downham reflected on how strategies and investments to build sustainable vaccine manufacturing capacities and capabilities will be structured. A mechanism contributing to the diversification and sustainability of vaccine manufacturing is technology transfers. Dr. Martin Friede (WHO) reported WHO has set up technology transfer hubs to expand access to know-how at the multilateral level. He highlighted the importance of the hubs providing know-how, standard operating procedures (SOPs) and licenses to practice the technology, not just for a single disease such as COVID-19, but to empower countries by providing the know-how to manufacture vaccines against disease targets that are a priority of the country.

Dr. David Robinson (BMGF) highlighted the need to move from 'build and decay' to 'build and sustain' in the context of manufacturing facilities. He suggested that facilities must be in continuous operation and generate revenue to at least cover the facilities fixed costs. Furthermore, facilities must produce routine vaccines in addition to those for pandemic responses and think regional or globally given that few countries have a domestic market large enough to generate sufficient revenue.

Dr. Morena Makhoana (Biovac) stated that the mechanisms that facilitated the growth of DCVMs in the past two decades are not necessarily sufficient to expand manufacturing on the African continent. Therefore, for the African continent to produce 60% of vaccines domestically by 2040 deliberate actions must be taken. Dr. Nicaise Ndembi (Africa CDC) added that collaborations and partnerships will underpin these deliberate actions and that all aspects of the value-chain must be considered. He reported eight ecosystem enablers for successful African vaccine production: agenda setting and coordination, market design and demand intelligence, access to finance, technology transfers and IP, regulatory strengthening, R&D, talent development, and infrastructure development.

Dr. Janet Byaruhanga (African Union Development Agency-NEPAD) shared plans for boosting local vaccine production in Africa. Citing the viability of manufacturing on the continent, Dr. Byaruhanga listed human resource development as a top priority, a point all panelists noted as critical.

10. Conclusion

In providing the meetings concluding marks, Rajinder Suri (DCVMN) thanked all speakers and participants for their engagement and contributions. He echoed the appreciation to DCVMN members for their efforts in mitigating the COVID-19 pandemic. Mr. Suri reiterated the importance of addressing vaccine inequity

to accelerate our way out of the pandemic. Partnerships and innovations have been, and will continue to be, critical in overcoming the current pandemic and preparing for future pandemics. As we move forward, DCVMN, working in collaboration with international stakeholders, is prepared to make an increasing contribution to protect all people against infectious diseases.

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The authors alone are responsible for the statements and expressed in this article, which do not necessarily represent the views, decisions or policies of any mentioned institutions mentioned in this report, or with which the authors are affiliated.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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