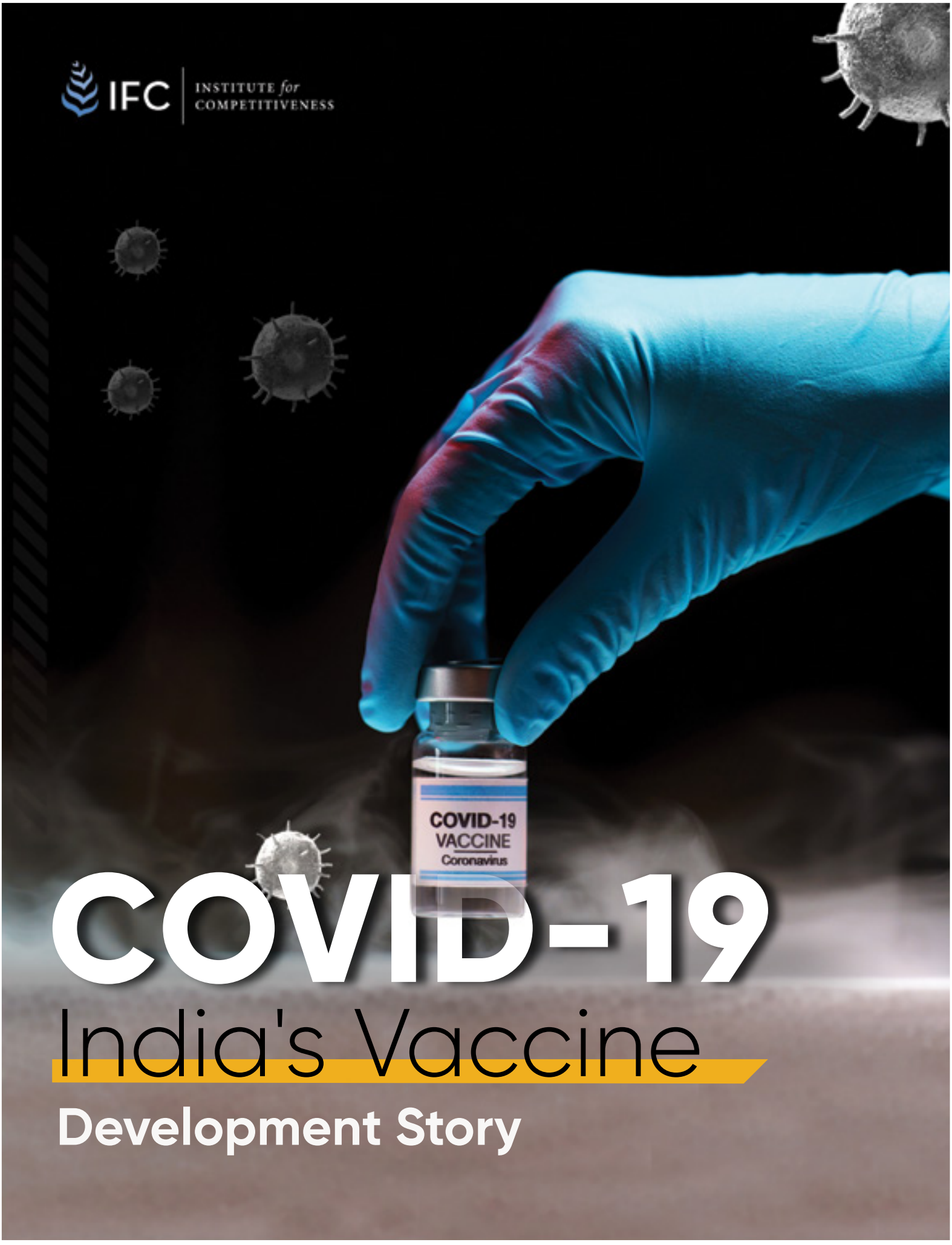
IFC | INSTITUTE for COMPETITIVENESS



COVID-19

India's Vaccine

Development Story

Note: This is an effort towards documenting covid response by Government of India. It is not a comparative statement or an endorsement of efforts by any of the entities mentioned in the report. The report cannot be construed as a Harvard or Stanford study

IFC | INSTITUTE *for* COMPETITIVENESS

COVID-19

India's Vaccine

Development Story

Authors

Amit Kapoor
Visiting Fellow and Lecturer,
Stanford University

Sandeep Goyal
Fellow,
Institute for Competitiveness

Designed By

litmus.ink

Table of Contents

Abbreviations

ABSL3	Animal Biosafety Level 3
AIs	Autonomous Institutes
AICTE	All India Council for Technical Education
AIIMS	All India Institute of Medical Sciences
AYUSH	Ayurveda, Yoga, Naturopathy, Unani, Siddha, Sowa-Rigpa and Homoeopathy
BBIL	Bharat Biotech International Limited
BCR	Block Control Room
BDO	Block Development Officer
BIBCOL	Bharat Immunologicals & Biologicals Corporation Ltd
BIRAC	Biotechnology Industry Research Assistance Council
BMGF	Bill and Melinda Gates Foundation
BSL3	Biosafety Level 3
BTF	Block Task Force
CDAC	Centre for Development of Advanced Computing
CDL	Central Drugs Laboratory
CDSCO	Central Drugs Standard Control Organisation
CoV	Coronaviruses
Co-WIN	Covid Vaccine Intelligence Network
COVID	Coronavirus Disease
CSIR	Council for Scientific & Industrial Research
CSO	Civil Society Organization
DBT	Department of Biotechnology
DCGI	Drug Controller General of India
DDH2020	Drug Discovery Hackathon 2020
DGHS	Director General Health Services
DHR	Department of Health Research

DNA	Deoxyribonucleic acid
DoP	Department of Pharmaceuticals
DRIVEN	DBT's Resource of Indian Vaccine Epidemiology Network
EUA	Emergency Use Authorization
FIRST Hub	Facilitation of Innovation & Regulation for Start-ups and Innovators Hub
FDI	Foreign Direct Investment
GCP	Good Clinical Practices
GoI	Government of India
i3	Innovate in India
I&B	Information and Broadcasting
IAP	Indian Academy of Paediatricians
ICGEB	International Centre For Genetic Engineering And Biotechnology
ICMR	Indian Council of Medical Research
ICDS	Integrated Child Development Services
ICU	Intensive Care Unit
IIL	Indian Immunological Ltd
IPV	Inactivated Polio Vaccine
ITSU	Immunization Technical Support Unit
JHU	John Hopkins University
JSI	John Snow Inc.
INSACOG	Indian SARS-CoV-2 Genomic Consortia
IRSHA	Interactive Research School for Health Affairs
ISL	Institute of Life Sciences
IMA	Indian Medical Association
MEA	Ministry of External Affairs
MeitY	Ministry of Electronics and Information Technology
MHA	Ministry of Home Affairs
MHRD	Ministry of Human Resource Development
MIC	Ministry of Education Innovation Cell

MIU	Mission Implementation Unit
MoD	Ministry of Defence
MoHFW	Ministry of Health and Family Welfare
MoHUA	Ministry of Housing and Urban Affairs
N-BRIC	National Biomedical Resource Indigenisation Consortium
NBM	National Biopharma Mission
NCC	National Cadet Corps
NCCS	National Centre for Cell Sciences
NCDC	National Centre for Disease Control
nCoV	novel Coronavirus
NEGVAC	National Expert Group on Vaccine Administration
NGO	Non-Government Organization
NIAB	National Institute of Animal Biotechnology
NIBMG	National Institute of Biomedical Genomics
NII	National Institute of Immunology
NIPERS	National Institutes of Pharmaceutical Education & Research
NIPR	National Intellectual Property Rights Policy 2016
NIV	ICMR's National Institute of Virology
NHP	National Health Policy 2017
NSDP	National Skill Development Policy
NSS	National Service Scheme
NTAGI	National Technical Advisory Group on Immunization
NYKS	Nehru Yuva Kendra Sangathan
PCV	Pneumococcal Conjugate Vaccine
PHEIC	Public Health Emergency of International Concern
PMBJP	Pradhan Mantri Bhartiya Janaushadhi Pariyojana
PM-CARES	Prime Minister's Citizen Assistance and Relief in Emergency Situations Fund
PPE	Personal protective equipment

PLIS	Production-Linked Incentive Scheme
PSU	Public Sector Undertaking
RCB	Regional Centre for Biotechnology
RCGM	Review Committee on Genetic Manipulation
RDIF	Russian Direct Investment Fund
REOI	Request for Expression of Interest
RFP	Request for Proposals
RIFC	Regulatory Information & Facilitations Centre
RISE	Rapid Immunization Skills Enhancement
RRSFP	Research Resources, Service Facilities and Platforms
RVV	Rotavirus vaccine
SDM	Sub-Divisional Magistrate
SOP	Standard Operating Procedure
SCR	State Control Room
SSC	State Steering Committee
SSI	Serum Institute of India
Td	Tetanus and adult diphtheria
TCV	Typhoid Conjugate Vaccine
THSTI	Translational Health Science And Technology Institute
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UK	United Kingdom
UNDP	United Nations Development Project
UNICEF	United Nations Children's Fund
UTF	Urban Task Force
VoC	Variants of Concern
WHO	World Health Organization
WTO	World Trade Organisation

Executive Summary

The first few cases of COVID-19 infection were reported in Wuhan, China on 31st December, 2019, which quickly snowballed into an outbreak, and before the world could respond, the coronavirus spread into different parts of the world, turning into a pandemic in January 2020.

The subsequent efforts made by the countries globally in making the discovery and development of COVID-19 vaccines, in a time-critical mode, have been significant in mitigating the biggest challenge faced by humankind. To contain the global spread of the outbreak, scientists, from across the world, acted with great urgency in discovering an effective cure. With the virus spreading at an exponential rate, the journey had been challenging, especially for developing countries like India that faced constraints due to limited resources and an overwhelming population.

India's first COVID-19 case was reported on 30th January, 2020. During the period between January to March of 2020, cases started increasing across the country and the situation became worrisome.

While the cases were still low in comparison to some other countries in the West, the Government of India (GoI) began to chart out an action plan to combat the pandemic. The unprecedented calamity threw up several challenges that pushed the GoI to take a multi-pronged approach — implementation of a nationwide lockdown; quickly ramping up health infrastructure; diagnostic and surveillance capacities; initiating indigenous R&D for treatment options; disseminating information on COVID appropriate behaviours so that people could protect themselves from the impact of virus. Acknowledged as the world's pharmacy and one of the most prominent vaccine manufacturers globally, India always had the significant role to play in the vaccine development and distribution at the global level. India's advantageous global position as a leading vaccine manufacturer, and in contrast, a vulnerable developing nation in the face of the pandemic, makes India a unique case and its journey of COVID-19 vaccine development and delivery is worth documenting.

India began efforts towards vaccine development in the early stages of the COVID-19 pandemic. The setting up of a high-level National Task Force in April 2020 for COVID-19 related works in the domain of science and vaccine development was a landmark decision in this regard. Co-chaired by Dr. V. K. Paul, Member (Health), NITI Aayog and Prof K. VijayRaghavan, Principal Scientific Adviser to the GoI, the task force aided the government in facilitating, keeping track of and monitoring the progress of national and international efforts in vaccine development. The task force consisted of experts and representatives from various relevant fields, thus allowing for multiple perspectives in decision-making and enabling better coordination among the various stakeholders.

In conjunction with actualizing an environment which fosters indigenous vaccine development, GoI also set out creating global tie-ups between Indian pharmaceutical companies and global vaccine manufactures

National efforts towards the development of the COVID-19 vaccine were led by Indian Council of Medical Research (ICMR) in association with BBIL. The partnership between these two entities, established on the 9th of May 2020, marks the beginning of the development process of Covaxin. ICMR spearheaded the COVAXIN development effort by isolating the SARS-CoV-2 virus, thereupon making India the fifth country in the world to attain this feat. ICMR also played a vital role of knowledge partner, accordingly sharing scientific wisdom by developing protocols and SOPs to be shared with BBIL as a part of technology transfer.
The Department of Biotechnology (DBT), assigned as the central coordinating authority by the task force, played a crucial in India's vaccine development journey. As the nodal agency, the DBT was tasked with identifying a pathway for vaccine development, making a dynamic list of national and international organisations working for vaccine development needs, monitoring their progress, and undertaking the multi-stakeholder facilitation at the government level.

In its own capacity, DBT began efforts towards COVID-19 vaccine research and development through initiatives like the COVID-19 Research Consortium and the National Biomedical Resource Indigenisation Consortium (N-BRIC). The DBT also set up an Empowered Committee, consisting of the Review Committee on Genetic Manipulation (RCGM) and Central Drugs Standard Control Organisation (CDSCO), to examine the applications for the development of vaccines, diagnostics, prophylactics, and therapeutics for the treatment of COVID-19, and recommending them approval within an agreed timeframe, in order to ease up the regulatory pathways and expedite the approval process of applications. The DBT launched the Rapid regulatory framework to further accelerate the processing of applications relating to recombinant vaccines against COVID-19.

India followed two strategic choices in COVID-19 vaccine development:

Vaccine Development Initiatives 1:

One of the choices was to foster indigenous vaccine development. Since India possessed the capacity and expertise to develop an indigenous vaccine, the GoI decided to incentivise innovation in this field. The Drug Discovery Hackathon 2020 (DDH2020), India's first ever national initiative for supporting drug discovery process, launched on 2nd July, 2020 was one of the initiatives in this direction.

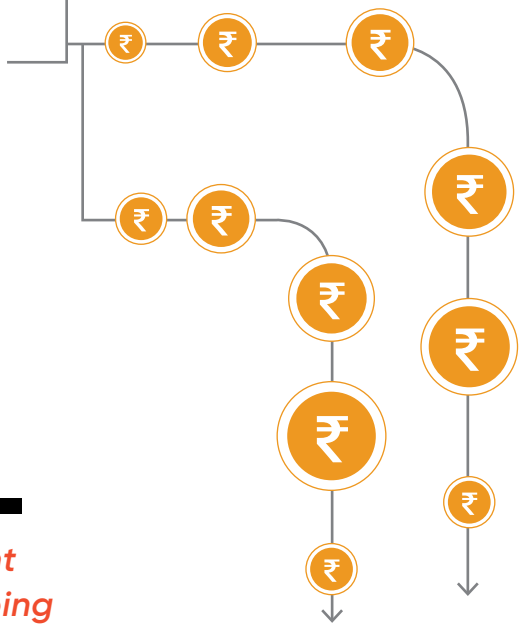
GoI's Rs 100 crores allocation from the PM-CARES fund and "Mission COVID Suraksha" gave further boost to indigenous innovators.

The leading vaccine candidate that emerged through this approach was Covaxin, developed jointly by Bharat Biotech International Limited (BBIL) and ICMR.

India's accomplishment in successfully developing not one but two vaccine candidates for the COVID-19 virus can be accredited to the several systemic interventions taken at the leadership level

Vaccine Development Initiatives 2:

As scientists across the globe were rigorously working towards vaccine candidates, with some making considerable progress, the GoI made the decision to push collaborations between Indian pharmaceutical companies and global vaccine candidates for India trials, technology transfer and mass manufacturing in India in case of global approvals and launch. Going for technology transfer agreements took the pressure off of indigenous vaccine developers and helped in hedging the risks related to vaccine development. In addition, early-stage tie-ups gave an opportunity to test potential vaccines in the country, which helped gauge the risks early as well as gave a push to the concerned regulatory body to ease up regulatory pathways. Serum Institute of India (SII) took the lead in this endeavour through its Oxford-AstraZeneca tie-up for manufacturing their vaccine in India with the brand name "Covishield".



Through both the processes of indigenous development and manufacture of vaccines through technology transfer, India was able to prepare two vaccines for its inoculation drive by the end of the year 2020- Covaxin and Covishield.

Each vaccine candidate's journey gives greater insight into the process that led to their success in rapid development and launch.

In the case of Covishield, the process began in April 2020 when SII joined the Oxford vaccine project as one of the seven global institutions

involved in manufacturing the vaccine. Later, a British pharmaceutical company AstraZeneca became University of Oxford 's vaccine manufacturing and distribution partner and entered into a licensing deal with SII. SII took a diversified approach in accessing the COVID-19 vaccine, and also tied up with the US-based biotech firm Codagenix and Austrian biotech company Themis Bioscience on two other COVID-19 vaccine candidates. An unprecedented move taken by SII was its decision to begin production of the Covishield vaccine post technology transfer from AstraZeneca/ Oxford University for Phase II and III trials in India, even as phase III clinical trials continued in the United Kingdom (UK). The decision gave the manufacturer head start on vaccine production, and the risk paid off as the vaccine candidate received approval for restricted use in January 2021.

In the development of Covaxin, BBIL approached ICMR to develop an inactivated vaccine after ICMR had successfully isolated the virus strain. While BBIL deployed the human resources and financial resources for the development of the vaccine, ICMR provided technical guidance and helped with preclinical studies and clinical trials. At the start of the process, both parties targeted a timeframe of 6-8 months for development, clinical trials, approvals and launch in India by the end of 2020, which encouraged them to work proactively, as well as seek fast-track approvals for trials. The accelerated regulatory processes cut down the timeline for vaccine development, and helped Covaxin to receive approval for restricted use in January 2021.

The approach taken by Covaxin and Covishield pushed India's manufacturers and regulators to realign their conventional development, testing, and assessment methods, thereby clearing the path for other potential vaccine candidates in the process. Further, for a populous country like India, two vaccine manufacturers were not sufficient to inoculate the whole population. Therefore, other vaccine candidates also started coming into the consideration list. The third vaccine candidate that received the DGCI's green light was Sputnik V, developed in Russia by Gamaleya Research Institute of Epidemiology and Microbiology and manufactured in India by Dr. Reddy's Laboratories as Russian Direct Investment Fund's (RDIF) Indian partner. Sputnik V received Emergency Use Authorization (EUA) on 12th April, 2021. At this stage, there were other vaccine candidates also in the pipeline, such as the Bio E Sub Unit Vaccine, Zydus Cadilla DNA Vaccine, BB Nasal Vaccine, and more.

However, India's battle against the COVID-19 pandemic did not end with the successful development of the vaccines. An equally huge challenge was the delivery of vaccines to over 1.3 billion people of India. Ensuring fair and equitable distribution was another

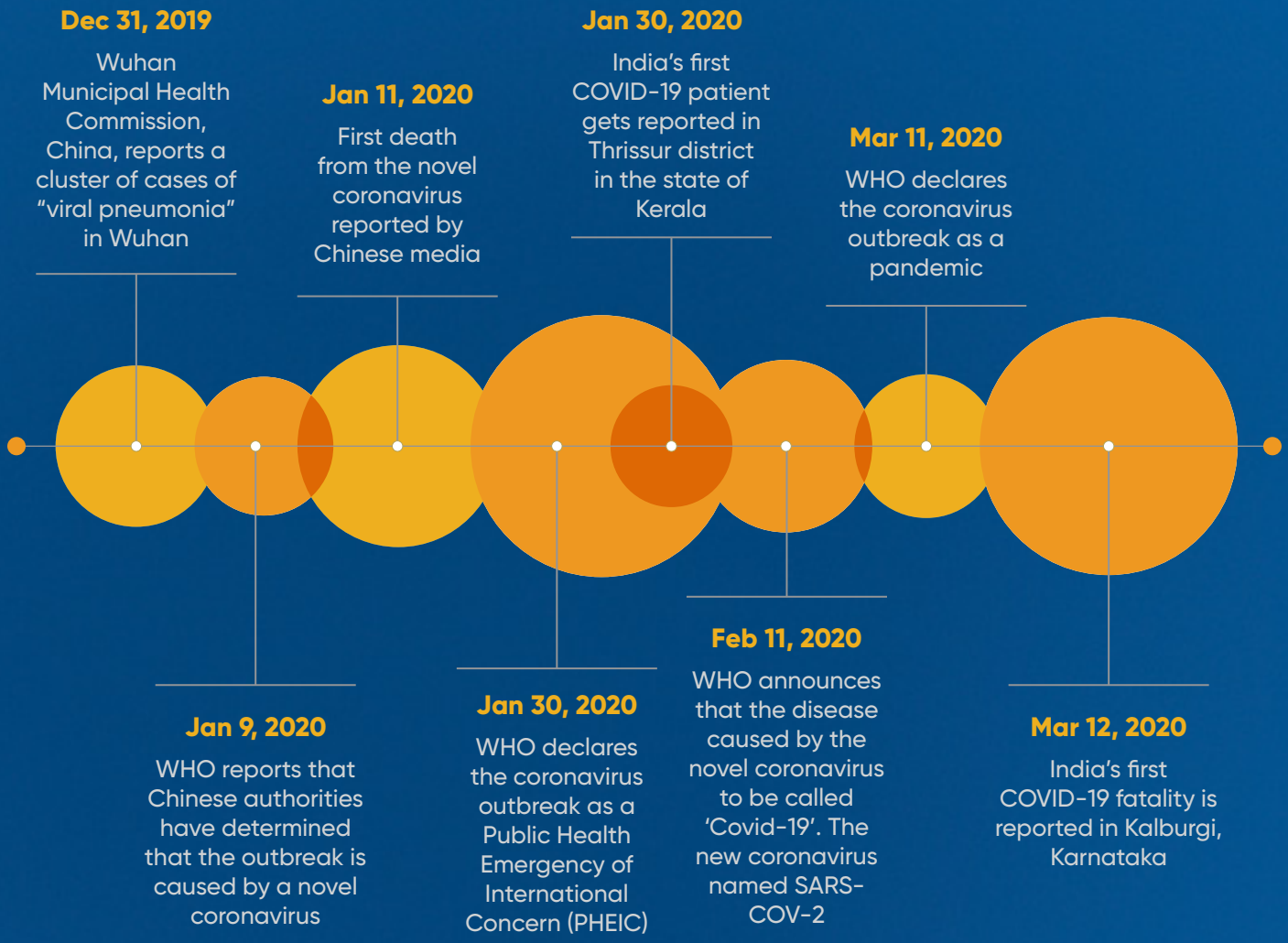
challenge and the prevalence of vaccine eagerness coupled with pockets of vaccine hesitancy due to the immense size and heterogeneity of the population further complicated the process. Prioritization of population groups, procurement strategies, pricing, cold-chain management and issues of logistics were some of the questions the GoI needed to tackle for the success of the COVID-19 vaccination journey. GoI began the implementation planning phase by setting up the National Expert Group on Vaccine Administration for COVID-19 (NEGVAC) committee on 12th August 2020 to oversee the vaccine roll-out strategy across India.

GoI undertook several dynamic initiatives encompassing all pertinent areas to vaccine administration, thereby strengthening India's readiness for vaccine delivery

01 Introduction

The genesis of COVID-19 goes back to the tail end of 2019, but this phenomenon only came to light on 31st December when World Health Organization (WHO) found the media statement by Wuhan Municipal Health Commission reporting a cluster of cases of "viral pneumonia" in Wuhan, China. (WHO, June 2020). However, nobody anticipated that this outbreak would mark the beginning of a global pandemic that would ravage the human civilization globally. In fact, at this point, even the cause of this "viral pneumonia" was unknown until Chinese authorities identified the infectious virus to be a novel coronavirus and reported it to the WHO authorities on 9th January. Before governments around the world could respond to this phenomenon, cases of infection began to appear globally across the countries. On 30th January 2020, WHO declared it a Public Health Emergency of International Concern (PHEIC), the same day India reported its first case in Thrissur, Kerala.

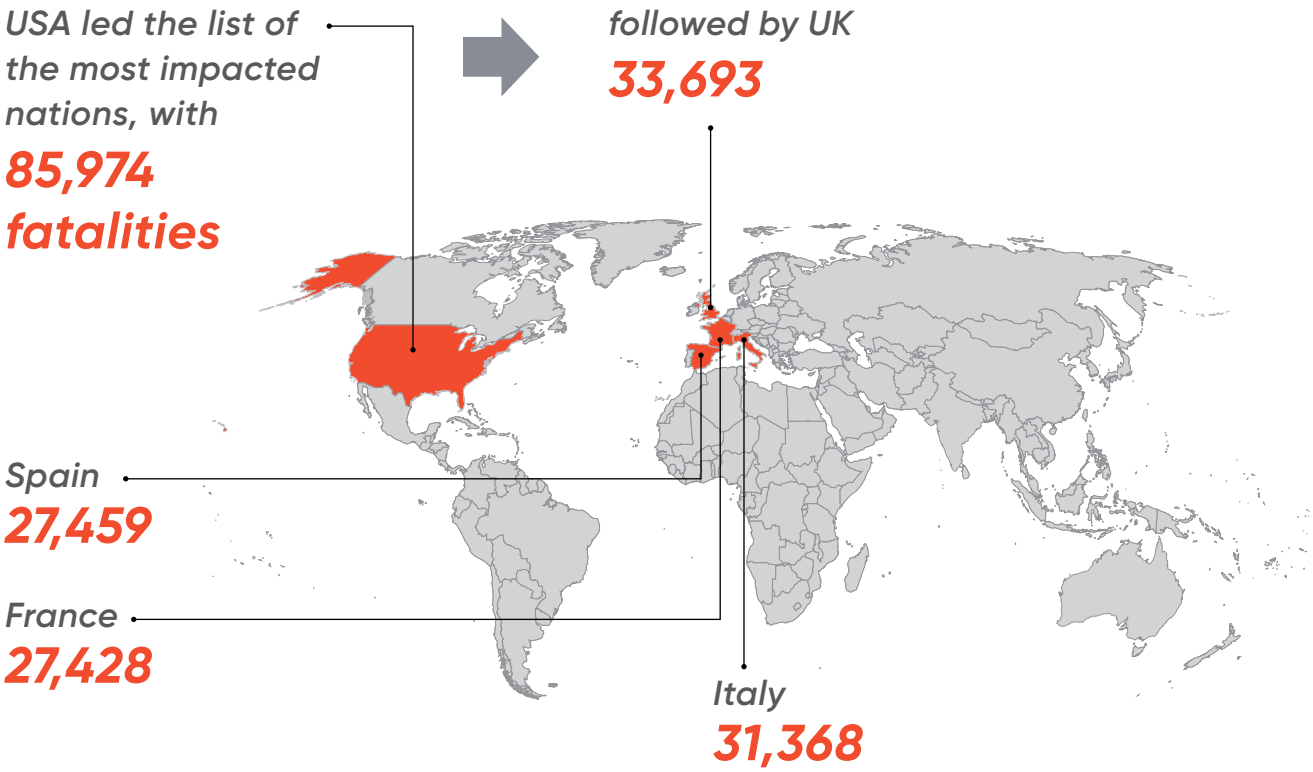
Table 1: Chronology Regarding Emergence of COVID-19



Source: Compiled by the Authors from Press Releases

As the virus took over the whole world, it was named 'COVID-19' on 11th February, 2020. By March 2020, cases had risen exponentially, creating widespread destruction in several countries. With no immediate cure in sight, governments started implementing radical social-distancing measures including nation-wide lockdowns and travel restrictions. According to the COVID-19 dashboard maintained by John Hopkins University (JHU), more than 4.48 million people in 188 countries got affected by the coronavirus during the first six months (December 2019 – May 2020) of the COVID-19 pandemic. This resulted in 0.3 million (6.7% of the reported cases) deaths globally, thereby creating a sense of fear and urgency (JHU, 4 May 2021).

The top five nations facing the maximum impact of COVID-19 outbreak in the initial six months accounted for 0.2 million of the 0.3 million deaths



Source: (JHU, 4 May 2021).

While the situation turned catastrophic in the West, the spread of the virus was relatively slower in India, along with the rest of South Asia (Brahma, Chakraborty, & Menokee, April 2020; Ramesh & Yadavar, April 2020). The situation in Iran and Italy served as cautionary tales, and India soon went into a nationwide lockdown on 25th March. However, despite strict lockdown protocols, cases gradually grew, and the healthcare infrastructure was stretched to its limit. Although the scientific community and the pharmaceutical industry had begun research on vaccine development, it was well-acknowledged this would be a long journey, and that a vaccine was not a possibility until at least the end of the year.

While vaccine development was underway, the government encouraged the adoption of the 3Ts strategy of 'test-track-treat' for early detection and containment of the pandemic until the fourth 'T' of 'Teekakaran' (vaccination) could come into play. Accordingly, India began to ramp up diagnostic and healthcare capacity. From civil administration, armed forces, railways, PSUs to private players, all came together to ramp up the country's healthcare infrastructure. In addition, the introduction of e-governance mobile app for real-time tracking and control of corona cases, indigenized manufacturing of PPE kits at par with WHO global standards, and localized manufacturing of testing swabs were also crucial efforts that turned the situation around for the better.

During this period, 27,360 ICU beds scaled up to 81,113. Similarly, India started from a single laboratory for COVID testing in January 2020 and scaled up to 2,288 laboratories by December 2020 (PIB release, 30 Dec 2020). The rapid scale-up of healthcare infrastructure was imperative in preventing the catastrophic situation in the first wave.

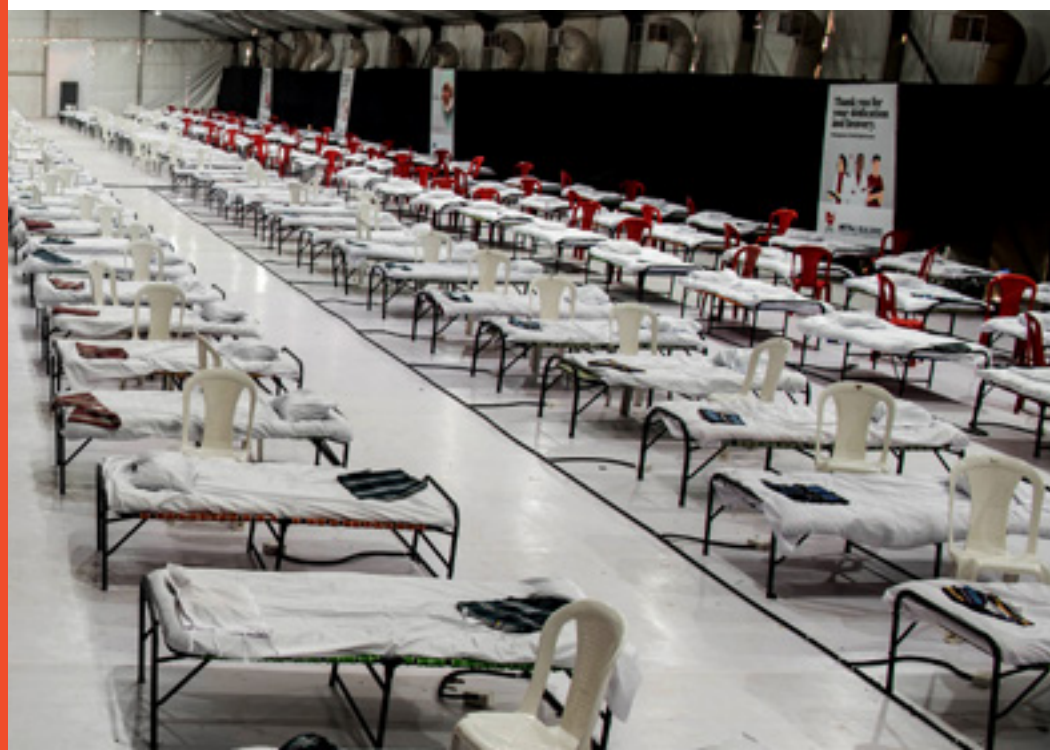
Nevertheless, the vaccine still holds out to be the most effective measure against a pandemic, and the only preventive one.

The surge in cases in April 2021 in India showed that implementing social distancing rules only brought behavioural change to an extent, and an improved healthcare sector too can reach its limits eventually. The trends across countries saw a significant change during May 2020 – April 2021. As on 4th May 2021, the total number of global cases reached 153.5 million resulting in 3.2 million deaths (JHU, 4 May 2021). The top five nations having the maximum number of COVID-19 deaths included the USA (32.47 million cases / 0.577 million deaths), Brazil (14.78 million cases / 0.408 million deaths), India (20.28 million cases / 0.222 million deaths), Mexico (2.35 million cases / 0.217 million deaths), and the United Kingdom (4.44 million cases / 0.128 million deaths) (JHU, 4 May 2021). Hence, the GoI together with the scientific community and the private sector had begun pushing for the development of vaccines since the onset of the pandemic.

As a result, oxygen-supported beds increased from

***62,458** on 21st April to*

***2,70,710** by 29th Dec, 2020*



India's case was unique in the sense that it faced twin challenges of inadequate healthcare infrastructure and a large population, including high population density. Being a developing nation, India's resource constraints also weighed heavily on the policy decisions. In light of these challenges, it becomes all the more important to bring out the country's vaccination journey in a detailed manner.

Hence, the purpose of this report is to present an in-depth documentation of India's COVID-19 vaccination journey that captures the process beginning from the initial stages of developing a comprehensive strategy for vaccines, the governance approach adopted by GoI, the role of each stakeholder including state governments and departments created in the process to the end stages of GOI tackling hurdles faced in the process and charting out the action plan for the pan-India roll-out of the vaccine.The layout of this report is divided into two parts: Part 1 chronicles the development and launch phase of COVID-19 vaccines in India and Part 2 focuses on the roll-out and delivery strategy of COVID-19 vaccines in India.

This document intends to serve as a repository for not only COVID-19 vaccine development and roll-out, but to also provide useful linkages regarding the systemic process towards the conceptualization of an idea, indigenized development, launch, and delivery ecosystem to tackle challenges arising in the future.

A complementary report will accompany this documentation effort, which will focus on the governance lessons learned from the pandemic. The purpose of the second report is to create a model of governance in times of crisis/ pandemics in the future. Hence, it will present key insights, strategies, challenges faced at the national and sub-national level and their success stories, notes on creating an ecosystem for crisis mitigation and navigating multiple stakeholders to achieve synergy of efforts, approach towards measurement and evaluation of the efforts undertaken, and so on.

02

India's Pharmaceutical Industry: Policy Support and Incentives

India's pharmaceutical industry is known as the world's pharmacy. It exports a significant volume of generic drugs and formulations to more than 200 countries globally (DoP Annual Report, 2020), and is the largest producer of vaccines. India is also coming up as a significant player in the area of pharma products-related contract manufacturing and research as well as manufacturing of biosimilars.

The GoI's enabling policies and schemes have been instrumental in incentivising the pharmaceutical industry to expand its horizons. Following are the key policy initiatives:

FDI policy:
As per the FDI policy, GoI has allowed 100% FDI under automatic route for greenfield projects and government route for brownfield investments as well as 74% FDI under automatic route for brownfield investments.

Pradhan Mantri Bhartiya Janaushadhi Pariyojana (PMBJP) 2015:
PMBJP, first launched as Jan Aushadhi Yojana in 2008 and later relaunched in 2015 provides generic drugs at lower prices to the masses while maintaining the quality and efficacy on par with the high-priced branded drugs. The product range constitutes of more than 800 medicines and 154 surgical and consumables, which are distributed pan-India via exclusive outlets called "Pradhan Mantri Bhartiya Janaushadhi Kendras"

- **National Skill Development Policy (NSDP):** NSDP involves setting up National Institutes of Pharmaceutical Education & Research (NIPERS) centres as innovation hubs for advanced research in pharmaceutical studies. As of now, seven NIPRES centres are operational in Ahmedabad, Guwahati, Hajipur, Hyderabad, Kolkata, Mohali and Raebareli.

- **National Intellectual Property Rights (NIPR) Policy 2016:** NIPR Policy was adopted by GoI in 2016 to recognize and promote India's Trade-Related Aspects of Intellectual Property Rights (TRIPS) compliant legislative framework for safeguarding the Intellectual Property Rights of the companies, thereby bringing India's IP regime in line with the global standards. It ensures compliance with the WTO's agreement on TRIPS.

- **National Health Policy (NHP) 2017:** NHP was launched by the GoI in 2017 as India's largest public health initiative aimed at ensuring universal health access to all rural and urban citizens of India.

Production-Linked Incentive Scheme (PLIS) 2021:
As part of AtmaNirbhar Bharat Abhiyan, The Union Cabinet cleared the PLIS to enhance the manufacturing and exporting capabilities of pharmaceutical companies in India. This involved an outlay of INR 15,000 Cr. for the pharma companies in India in the years to come (Invest India Website, May 2021).

National Biopharma Mission (NBM) 2017:

NBM, an industry-Academia Collaborative Mission, was launched with the aim to accelerate biopharmaceutical development in the country. Under the Mission, Innovate in India (i3) programme was launched to create an enabling ecosystem to promote entrepreneurship and indigenous manufacturing in the sector.

Promotion of biotechnology:

The DBT has a slew of programmes and schemes that aim to promote biotechnology in India. Biotechnology Parks/Incubators have been established in different parts of the country that provides the necessary infrastructure to convert research into products and services. Biotechnology is also one of the champion sectors under the Make-in-India initiative, which led DBT to get Biotechnology Industry Research Assistance Council (BIRAC) to establish Biotechnology Industry Facilitation Cell. Another notable initiative by DBT is the Research Resources, Service Facilities and Platforms (RRSFP) program for promotion, upgrade and establishment of new biotech facilities/ infrastructure in research institutions or universities.

Key Pharmaceutical Clusters and Companies in India

Indian pharmaceutical companies have shown a distinct orientation and preference towards working in clusters as it eases out the operational challenges in terms of skilled manpower, raw material inputs, logistics and transportation as well as other support services. Such industry clusters have been developed in multiple regions across India. Table 2 below elaborates the emergence of pharmaceutical clusters or zones for different types of pharma product offerings.

Table 2: Pharmaceutical Clusters / Zones in India

Pharmaceutical Units - Categories	Industry Zones / Clusters – Key Locations
Captive R&D Units	Delhi (NCR), Ahmedabad (Gujarat), Pune (Maharashtra), Hyderabad - Medak (Telangana), Mysuru (Karnataka), Chennai (Tamil Nadu)
Contract R&D Units	Ankleshwar (Gujarat), Mumbai (Maharashtra), Hyderabad - Medak (Telangana), Bengaluru (Karnataka), Chennai (Tamil Nadu)
Established Bulk Drugs Cluster	Vapi, Baroda (Gujarat), Tarapur (Maharashtra), Hyderabad – Medak (Telangana), Bengaluru (Karnataka), Chennai (Tamil Nadu)
Established Formulations Cluster	Aurangabad (Maharashtra), Hyderabad – Medak (Telangana)
Emerging Bulk Drugs Cluster	Vizag (Andhra Pradesh)
Emerging Formulations Cluster	Baddi (Himachal Pradesh), Pantnagar (Uttarakhand), Sikkim, Andhra Pradesh, Puducherry

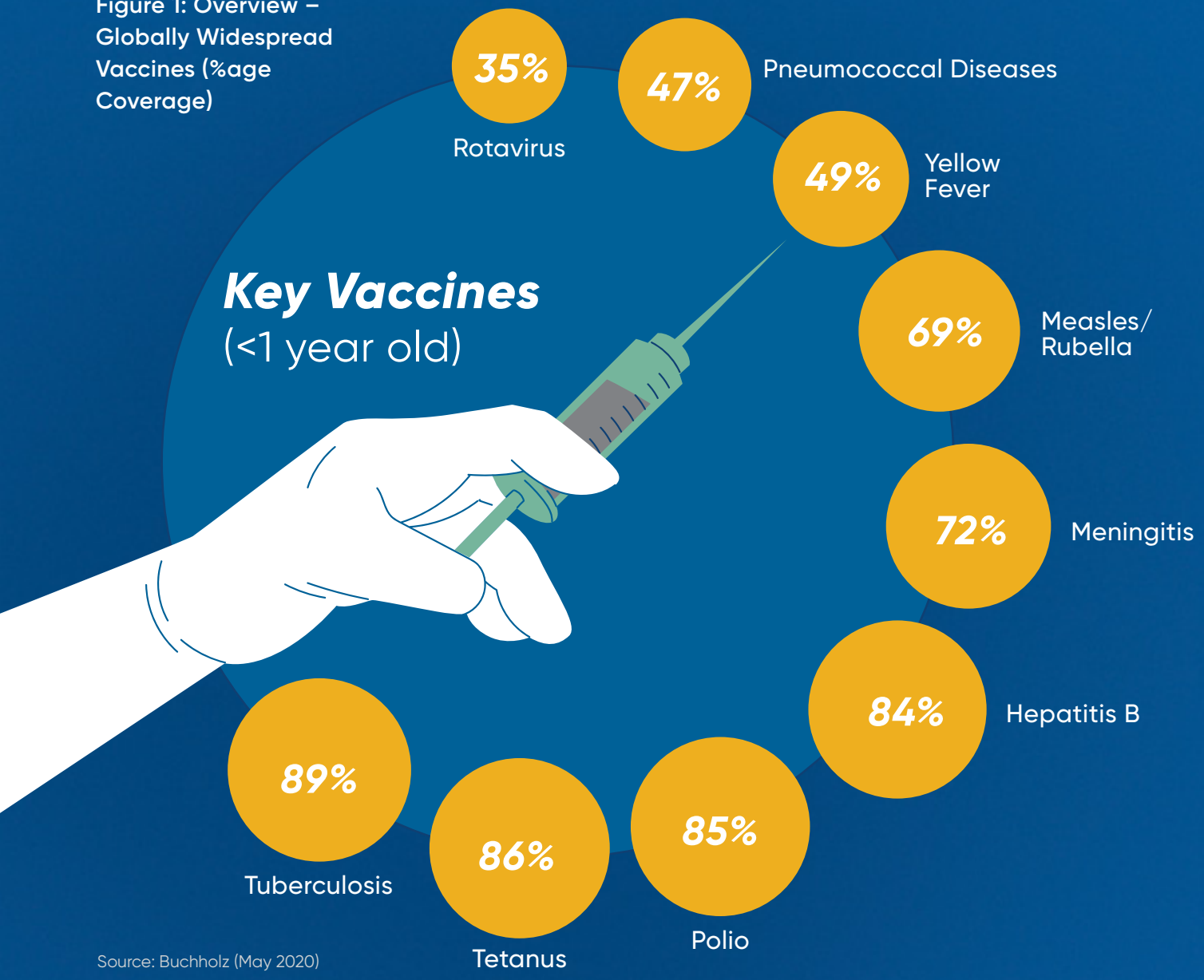

CLEANED
FROZEN

03

COVID-19 Vaccine Development: A Global Overview

According to World Health Organization (WHO), vaccination is among the most important developments in human history, saving as many as 3 million lives every year (Broom, June 2020). There had been several diseases in the 20th century, which caused a very high rate of morbidity among the masses and ultimately got controlled by vaccine-based intervention. Figure 1 illustrates some of the key vaccines over history and their coverage across the world.

Figure 1: Overview – Globally Widespread Vaccines (%age Coverage)

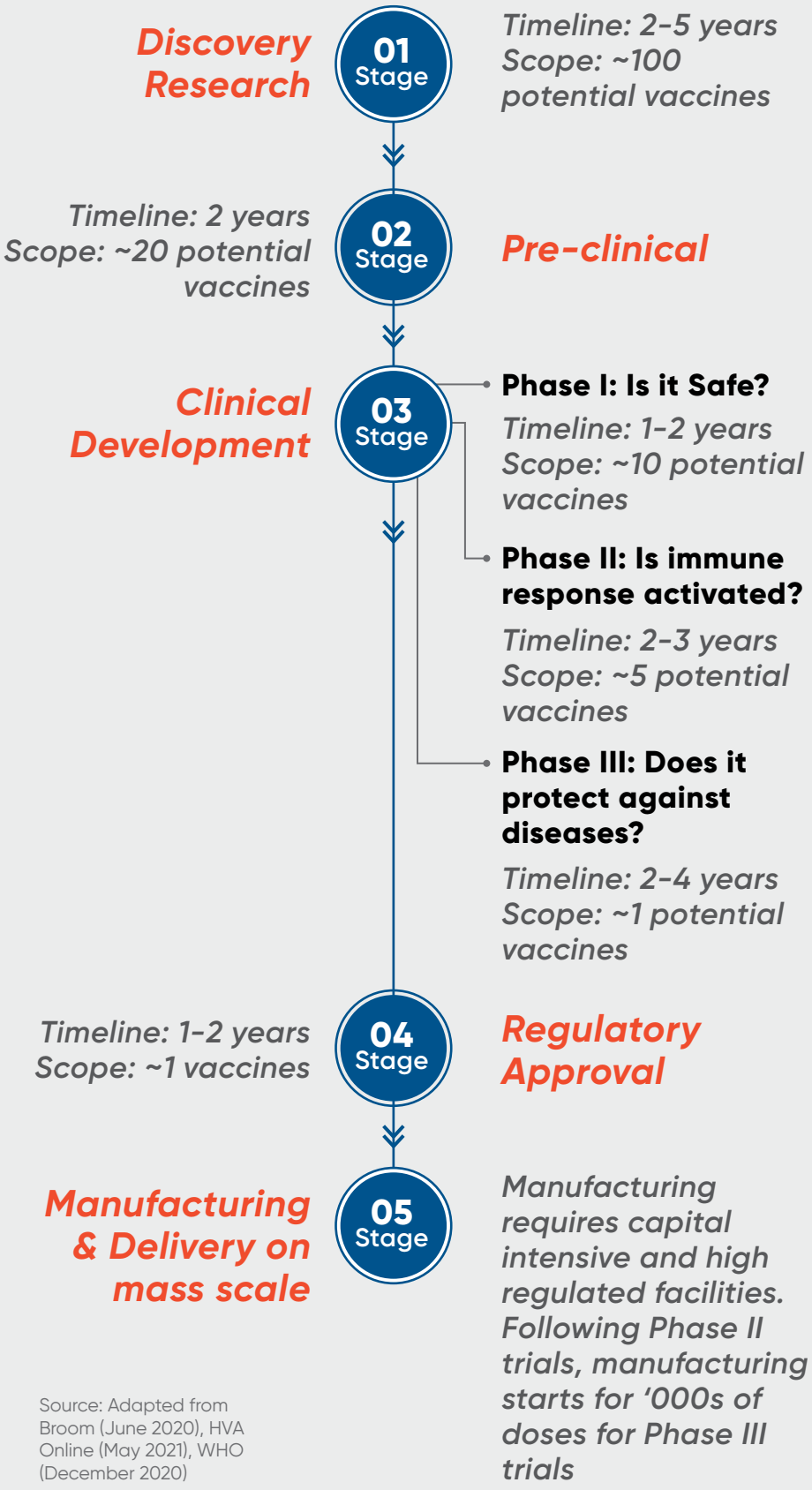


Source: Buchholz (May 2020)

COVID-19 pandemic has proved to be a gamechanger for the world in every way, including in the field of vaccine development. On one hand, the unprecedented calamity disrupted normal life and resulted in a loss of many lives, but on the other hand, it also spurred among humans a stronger sense of determination and the willingness to persevere against all odds, and drove innovation in all spheres. One of the key examples was the development and launch of the COVID-19 vaccine by pharmaceutical industry players in a record time of

8 months (Sethu, Feb 2021). Typically, vaccine development involves a large timespan of 8-10 years for development considering the need for efficacy, safety and immunogenicity. In the case of, COVID-19 pandemic situation wherein millions of people were getting affected globally, there was no such liberty of undertaking the vaccine development in 5-6 years. To give a better perspective on the time period of vaccine development, it typically involves a research and development life-cycle of around ten years and costs around $500 million before it reaches the stage of approval and mass manufacturing (Broom, June 2020). Furthermore, a new vaccine carries on average a failure rate of 93% between animal studies/trials and final product registration.

Figure 2: General Vaccine Development Process (~$500 million, ~10 years)



Source: Adapted from Broom (June 2020), HVA Online (May 2021), WHO (December 2020)

One of the key success factors, which led to the development and launch of COVID-19 vaccine within a year involves the use of new platforms and technologies for vaccine development.

Traditionally, vaccines were developed for a specific disease as live-attenuated, inactivated, or sub-unit vaccines. Viral-vectored and mRNA platforms are newer technologies that have been used in developing COVID-19 vaccines. The different technology types used by the COVID-19 vaccine manufacturers include mRNA (Pfizer–BioNTech, Moderna), Adenovirus vector (Oxford–AstraZeneca, Sputnik V, Johnson & Johnson, Convidecia), Inactivated virus (Sinopharm – BBIBP, Sinopharm – WIBP, CoronaVac, Covaxin, CoviVac, QazVac), and Protein subunit (CIBG-66 - ABDALA, EpiVacCorona, RBD-Dimer) (WHO, Jan 2021; U.S. Department of Health and Human Services, 2021; Craven, June, 2021). Besides the new platforms and technologies, all the countries involved in vaccine development adopted the fast-track approach with due coverage of scientific and precautionary protocols. Based upon the field results in terms of minimal adverse events and rapid scale of vaccination since January 2021, it is quite evident that fasttrack COVID-19 vaccine development did not compromise on the efficacy, safety and immunogenicity guidelines despite shortening the development time-lines to 6-9 months.

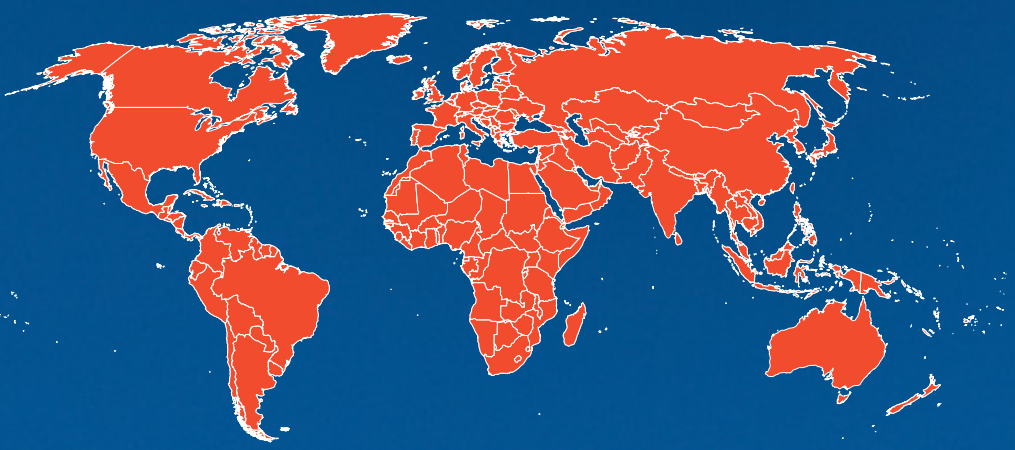
Annexure 1 provides an overview of the various types of vaccine platforms.

04 Global Access Strategies

Mid-way during the vaccine development phase in 2020, there was a huge dilemma among the nations globally as to how to get first access to sufficient volumes of COVID-19 vaccines for their citizens. The vaccines were required by the majority of age groups across countries and that too on a time critical basis. Also, there was widespread uncertainty regarding which candidate would emerge successfully in the development and mass-scale launch process of COVID-19 vaccine.

Considering the enormity of demand for vaccination across the countries globally as well as uncertainty regarding the successful development of the vaccine by a specific company, varying access strategies were adopted by countries to get the first-mover advantage in respect to the access to vaccine or vaccines having regulatory and WHO approvals. The most common access mechanism adopted by a majority of the big countries including India, involved the dual access model wherein countries incentivised the local pharmaceutical companies to develop their own vaccine with the support of Government R&D organizations and/ or sign the licensing agreement with global vaccine candidates, which are undergoing Phase I, II, III trials (Deo et al., July 2020).

Some of the wealthy nations entered into unilateral pre-purchase agreements with COVID-19 vaccine manufacturers. This approach, also dubbed as "vaccine nationalism" was also practised during the 2009 H1N1 flu pandemic when the USA acquired exclusive access to 0.6 million doses out of the two million doses, which were available for the flu pandemic (Deo et al., July 2020). Other wealthy European nations also negotiated access to exclusive access to H1N1 flu doses during the same time-period. These nations then shared the remaining surplus with the developing and undeveloped nations. However, this approach can delay equitable and timely access to the life-saving vaccine or drug for the people living in non-wealthy nations, thereby creating a huge socio-economic impact on these nations. The practice of "vaccine nationalism" can also be detrimental to even the nations practising it. As historical evidence suggests, as referenced by Dr. Harsh Vardhan, the children of the entire world had to be vaccinated against Poliomyelitis only because Pakistan and Afghanistan were unable to vaccinate their citizens, despite Polio being eradicated from the rest of the world. Likewise, countries cannot be safe from COVID19 if the disease still prevails in any part of the world (PIB release, 7th March)



Global vaccine access was also influenced by the export decisions of nations that were having the raw materials used towards the development of COVID-19 vaccines, especially in case the of nations that are dependent on such imports. India's vaccine development efforts too were similarly influenced when the USA temporarily restricted the export of the critical raw material for COVID-19 vaccine, which was urgently required by Serum Institute of India (SII) for ramping up the production of Covishield based on viral-vectored technology. During January 2021 - April 2021, the US Administration invoked US Defense Production Act, 1950 in order to ban the export of critical raw materials outside the country and use them instead for the fulfilment of federal contracts (Raghavan, April 2021). The US President invoked this embargo on the export of critical raw materials like plastic bags, filters and cell culture media. These raw materials were used by the majority of the COVID-19 vaccine manufacturers especially those making use of viral vector, inactivated, protein subunit, and mRNA technologies. Table 3 provides the details regarding critical raw materials used during the manufacturing of the COVID-19 vaccine.

According to the US administration, US Defense Production Act was invoked in order to ensure the 24*7 uninterrupted supply of critical raw materials to the US vaccine manufacturers including Pfizer, BioNTech, and Johnson & Johnson (Raghavan, April 2021; Sirur, April 2021). According to a report by the World Trade Organization (WTO), a typical vaccine manufacturing plant needs around 9,000 different raw materials, which are sourced from 300 key suppliers across 30 countries (Raghavan, April 2021). Any delay or bottleneck or export restrictions on the supply of these raw materials, especially the critical ones directly affect the scaling up and supply logistics for the vaccine makers. The same was experienced by SII due to the restrictions posed by the USA on plastic bags, filters and cell culture media. Specific companies in certain countries have competency in manufacturing raw materials used in the production of COVID-19 vaccines and thereby it becomes difficult to find an alternative during a pandemic.

Table 3: COVID-19 Vaccines – List of Critical Raw Materials

Raw Material Type	Description	Vaccine Technology
Bio Reactor Bag	A disposable bag is used for artificially growing large quantities of cells used to cultivate the viruses required for the vaccine. Also, saves time between batch production by eliminating the need to clean and sterilize the bioreactor vats.	Inactivated, Viral Vector, Protein Subunit, mRNA
Filter	Comes in different pore sizes and allows purification and sterilization of the vaccine after virus cultivation.	Inactivated, Viral Vector, Protein Subunit, mRNA
Cell Culture Media	Liquid gel which helps in the growth of cells in the lab by enriching them with required nutrients.	Inactivated, Viral Vector, Protein Subunit
Lipid Nano Particles	Rely on materials like non-animal-based cholesterol and equipment as microfluid and nanofluid mixers to encapsulate the drug substance for delivery.	mRNA
Microcarriers / Microcarrier Beads	Used for growing protein-producing or virus generating cells during vaccine production.	Inactivated, Viral Vector, Protein Subunit

05

COVID-19 – Vaccine Development and Access in India

Since the increased incidence of coronavirus cases in March 2020 - May 2020, GoI had begun taking steps towards the development of a vaccine. The GoI realised very early on that control and mitigation steps like nation-wide lockdowns, use of N-95 masks, and Personal Protective Equipment (PPE) kits etc. were essential yet temporary measures in controlling the spread of coronavirus. With the pandemic inducing many economies to impose export restrictions, India's need to become self-reliant also provided a stronger momentum to the Aatmanirbhar Bharat mission, and pushed India towards developing vaccines in its own capacity

Furthermore, as one of the biggest vaccine manufacturers in the world, it was evident that India would have a big role to play in the development of the COVID-19 vaccine.

India's success in producing vaccines like the Inactivated Polio Vaccine (IPV), Rotavirus vaccine (RVV), Pneumococcal Conjugate Vaccine (PCV), Typhoid Conjugate Vaccine (TCV), Tetanus and adult diphtheria (Td) vaccine in the recent past were a testament to India's importance in vaccine production.

India also houses the world's largest vaccine manufacturing facility owned by the Serum Institute of India (SII), which is also the world's largest vaccine manufacturer by number of doses produced and sold globally. Thus, India already had a strong groundwork for manufacturing COVID-19 vaccines (Nair, Sept 2020). In addition, the prequalification awarded by WHO to India's first indigenously developed rotavirus vaccine, ROTAVAC by BBIL in 2018 was a notable achievement (Bharat Biotech, Jan 2018), proving that India could even develop another indigenous vaccine this time, against COVID-19.
Besides having the capacity to develop vaccines, the urgency of developing one in the face of rapidly rising cases of coronavirus was a catalyst in the process. The GoI was up against an invisible enemy but determined to protect as many lives as possible. The challenge was the race against time, limited resources and meeting the demand for vaccination at such a large scale, i.e., by 100% of Indians. As part of the ***Aatmanirbhar Bharat mission***, India was able to develop an indigenous supply chain of high-quality PPEs and testing swabs from scratch (Kapoor & Goyal, Oct 2020), which proved that vaccine development and delivery against the coronavirus was also possible with methodical planning and collaborative efforts. All these experiences and achievements sowed the seeds for a "Made in India" vaccine.

India's approach towards COVID-19 vaccine development can be looked at from three dimensions. The first dimension highlights the GoI's first response in terms of setting up a Task Force to review and manage works

related to COVID-19 vaccine development. The second dimension elaborates the role of two "Made in India" vaccines, COVIDSHIELD and Covaxin as front-runners in driving vaccine development, mass manufacturing and inoculation capabilities of India thereby enabling access to COVID-19 vaccines for millions of people in India by January 2021. The third dimension looks into the stage of regulatory approvals and the emergence of other potential vaccine players who will be setting up the mass manufacturing facility in India during the second wave of COVID-19.

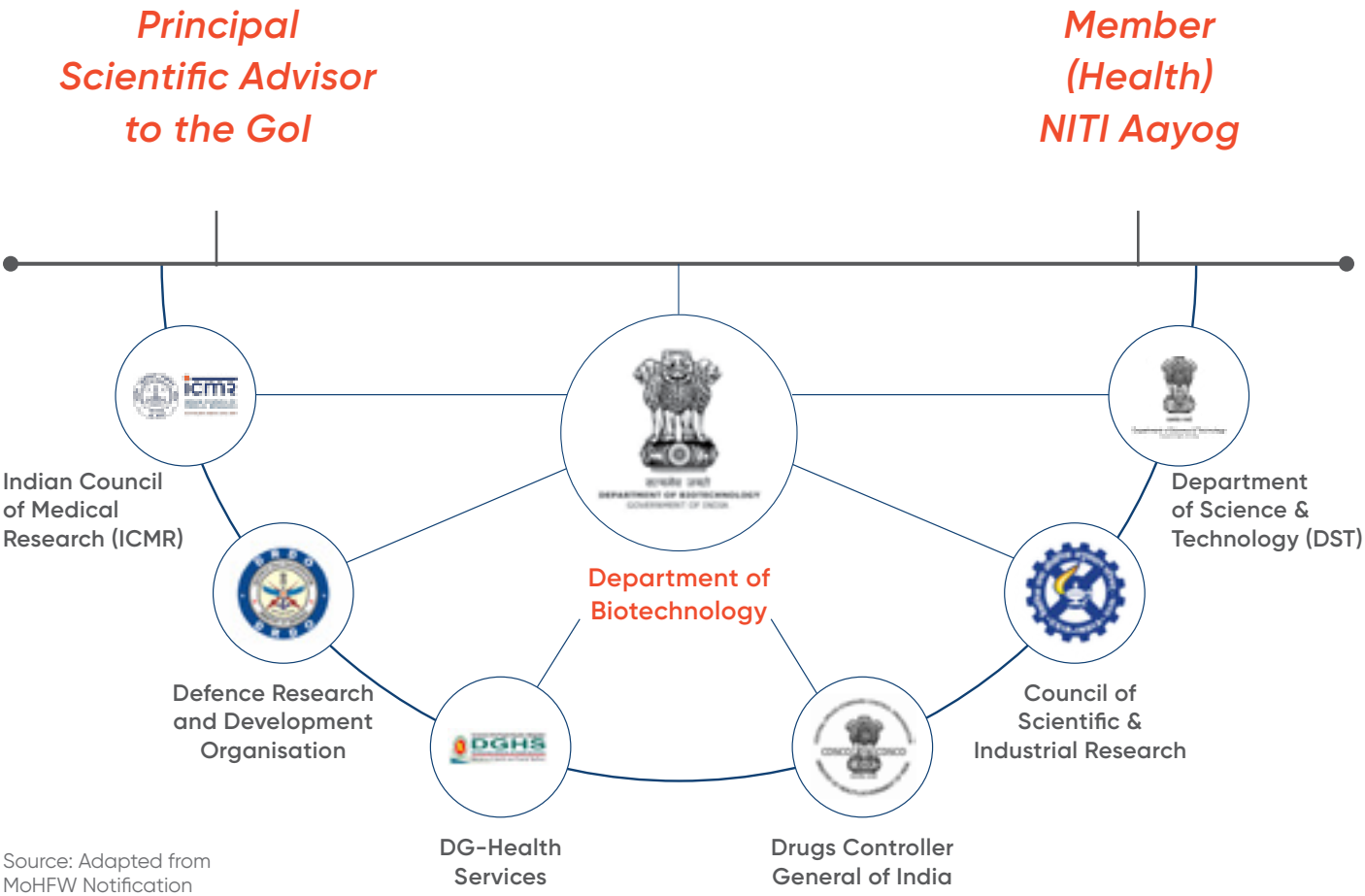
The First Response – Setting up the Task force for Vaccine Development and Access

As early as April 2020, the GoI began to review vaccine development efforts by Science & Technology institutions along with other efforts to deal with COVID-19, in the areas of diagnosis, drugs, hospital equipment accessories and general wellness.

The Government brought together the best minds of India having the necessary knowledge, skills, and experience to develop the vaccine for the pandemic situation. NEGVAC (National Expert Group for Vaccine Administration) was set up under MoHFW to lead the vaccination initiative for the masses in India.

On April 19, 2020, the GoI set up a high-level task force for COVID-19 related works in the fields of science and vaccine development. (MoHFW Notification, 19 April 2020a) Co-chaired by Dr. V. K. Paul, Member (Health), NITI Aayog and Prof K. VijayRaghavan, Principal Scientific Adviser to the GoI, the task force also includes representatives from AYUSH, ICMR, Department of Science and Technology (DST), Department of Biotechnology (DBT), Council of Scientific and Industrial Research (CSIR), Defence Research and Development Organisation (DRDO), DG-Health Services and Drug Controller General of India (DCGI) as its members. (MoHFW Notification, 19 April 2020a) Through the Task Force, the Government further facilitated, kept track and monitored the progress of national and international efforts in vaccine development, as the Task Force created "clinical cohorts" focussing on long-term follow up of people for having a better understanding of disease and management. Refer to Figure 3 for a detailed overview of the Task Force set up by GoI for indigenous vaccine development initiative.

Figure 3: COVID-19 Vaccine Development in India –Setting up the Task Force



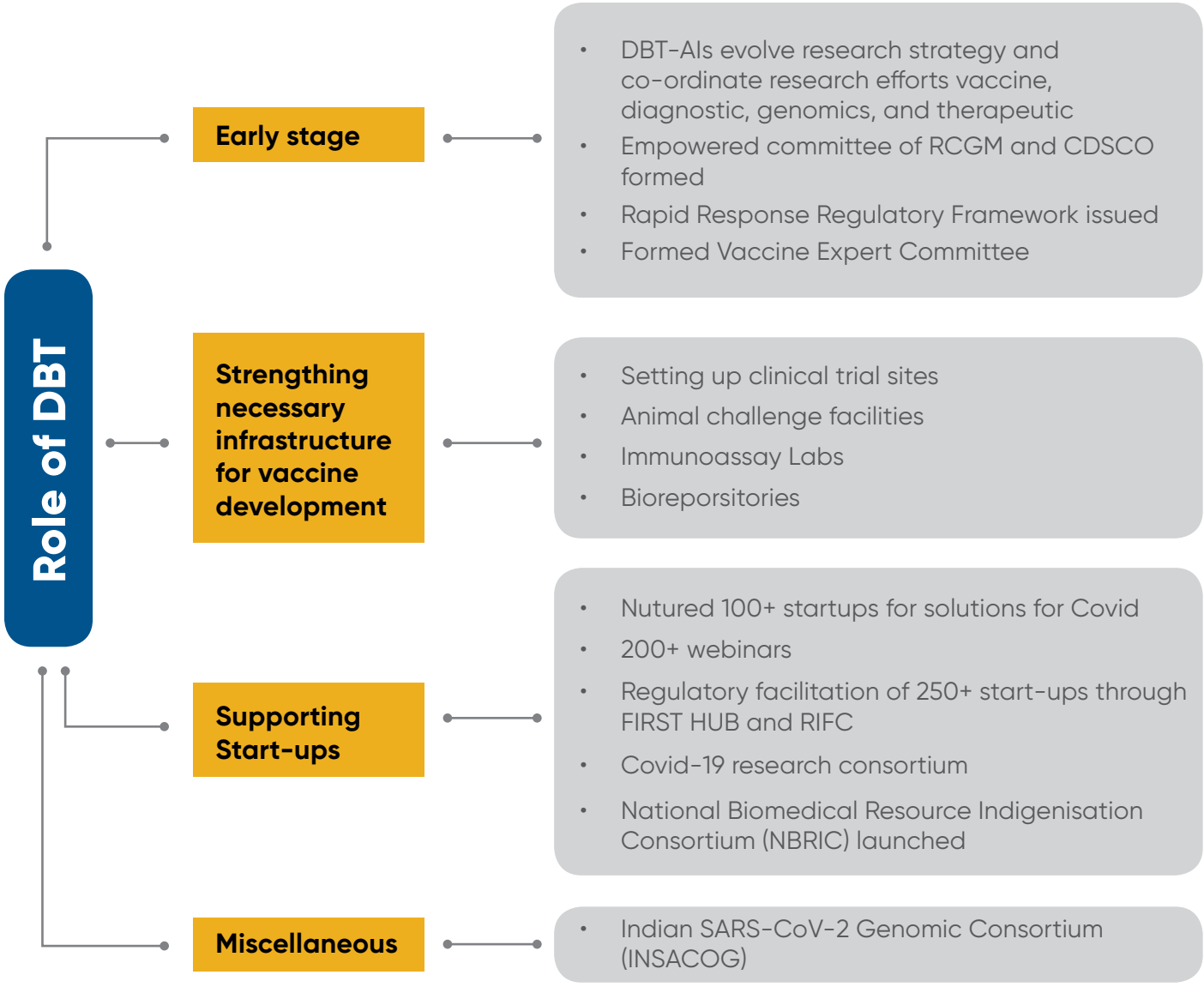
Source: Adapted from MoHFW Notification (19 April 2020a)

The Task Force made DBT a central coordinating authority, wherein they were tasked with identifying a pathway for vaccine development. As the nodal agency, they were assigned the work of making a dynamic list of national and international organisations working for vaccine development needs, monitoring their progress, and undertaking facilitation at the government level. In fact, even before the formation of the task force, DBT had already initiated efforts towards COVID-19 vaccine research and development.

Role of DBT

The DBT took on an all-encompassing role to fulfil, ranging from facilitating research, streamlining regulation to enabling a supporting ecosystem as well as extending support to start-ups engaged in developing COVID solutions. DBT played a crucial role in the development of vaccines. Over the course of the pandemic DBT funded the development of more than 15 vaccine candidates, ensuring support for the clinical trial sites, immunoassay labs and animal challenge models. Therefore DBT aided all vaccine candidates along their development process. DBT especially contributed towards the development of COVAXIN by providing Bharat Biotech with funding support. COVAXIN was jointly developed by ICMR and BBIL. Both entities played an equally important role in the development of COVAXIN and DBT closely monitored the vaccine development process. Figure 4 provides an overview of the DBT's initiatives and efforts.

Figure 4: DBT – Roles and Responsibilities During COVID-19 Vaccine Development



Early stages of Indigenous Vaccine Development

In one of the earlier instances of efforts undertaken by the DBT, the first discussion meeting with Autonomous Institutes (AIs) of DBT regarding the current novel Coronavirus infection was held on 6th February, 2021, wherein scientists from the National Institute of Immunology (NII), Translational Health Science And Technology Institute (THSTI), National Institute of Biomedical Genomics (NIBMG), Regional Centre for Biotechnology (RCB), International Centre For Genetic Engineering And Biotechnology (ICGEB), and officials of DBT-BIRAC participated to evolve a research strategy to be undertaken by the DBT pertaining to the development of vaccines for COVID-19.

Recognizing the need for immediate research and product development to combat the disease, DBT set up an Empowered Committee consisting of the Review Committee on Genetic Manipulation (RCGM) and Central Drugs Standard Control Organisation (CDSCO) on 20th March, 2020. The committee was tasked with examining the applications for development of vaccines, diagnostics, prophylactics, and therapeutics for the treatment of COVID-19 and recommending them approval within an agreed timeframe, in order to ease up the regulatory pathways and expedite the approval process of applications (DoBT, March 2020).

By the end of May 2020, DBT came out with the Rapid Response regulatory framework for fast-track processing of applications relating to recombinant vaccines for COVID-19, based on the recommendation of the Empowered Committee of RCGM and CDSCO. These steps undertaken for streamlining the biosafety regulations facilitated the ongoing research work on vaccine development. As the national regulatory body for pharmaceuticals and medical devices, CDSCO played an instrumental role in ensuring safety protocols are followed at all stages of vaccine development while also ensuring that delays are not caused in the process.

To support researchers and industries involved in research on COVID-19, the following Biosafety Regulations for COVID-19 were issued by RCGM and DCGI:

a. Rapid Response Regulatory Framework: to provide expedited regulatory approvals for all diagnostics drugs and vaccines
b. Regulations and Guidelines for recombinant DNA Research & Biocontainment-Interim Guidelines of laboratory biosafety to handle COVID 19 specimens for R & D purpose
c. A Rapid Response Regulatory Framework for COVID 19 Vaccine development.

The DBT also worked with the NITI Aayog to provide guidelines for sharing Bio-specimen & Data for Research on COVID-19. Further, to help research groups and vaccine developers meet regulatory requirements with the DCGI, DBT also formed a COVID-19 Vaccine Expert Committee, which met every two weeks and provided them with scientific and technical inputs. The committee held its first meeting on 28th July 2021 (Pilla, December 2020).

Strengthening necessary infrastructure for vaccine development

Vaccine development is a multi-stage process that cannot be successful without a strong enabling ecosystem, which includes pre-clinical trials involving small animals for evaluating the safety and potential of the vaccine candidate in preventing disease and later, clinical trials involving humans for assessing the safety and immunogenicity of the vaccine as well as its efficacy across population groups. The clinical trials itself are conducted across multiple phases – three, to be precise – and its results determine whether the vaccine should be approved for distribution or not. As companies raced to develop a vaccine against SARS-CoV-II, India required a large network of clinical trial sites to facilitate the approval process. Under DBT's Resource of Indian Vaccine Epidemiology Network (DRIVEN), five Good Clinical Practices (GCP)-compliant trial sites for Phase III clinical trials were prepared by the end of July 2020 (Raghavan, July 2020), with each site having access to a cohort of about 50,000 – 1,00,000 healthy volunteers, who could be tracked for prolonged periods of time. These sites were INCLEN Trust International, Palwal; KEM, Vadu, Pune; Society for Health Allied Research (SHARE), Hyderabad; National Institute of Epidemiology, Chennai and Christian Medical College (CMC), Vellore) and six Demographic Health Sites (DHS) (DBT, 2021). By June 2021, DBT reported setting up nearly 54 GCP Compliant clinical trial

sites across the country. Along with clinical testing, DBT was also involved in facilitating pre-clinical studies. Hence, recognizing the need for preclinical research on in vitro and model organisms, DBT's autonomous research institute, Institute of Life Sciences, Bhubaneswar, established animal models and an animal biosafety level 3 (ABSL3) laboratory for the same in June, 2021 (MST Notification, June 2021). This was initiated under the GoI's Mission COVID Suraksha and supported by BIRAC. Besides ILS, three other DBT AIs provided animal challenge facilities for generating animal models for SARS-CoV-2, namely THSTI Faridabad, inStem Bengaluru and NII New Delhi.

One of the bottlenecks in vaccine production in India pertained to the vaccine testing infrastructure. The Central Drugs Laboratory (CDL) in Kasauli, Himachal Pradesh, has been the only vaccine testing laboratory in India testing the batches of COVID-19 vaccines along with other vaccines. It is the National Control Laboratory, which issues testing and pre-release certification of immunobiological (vaccines and antisera) meant for human use in India. Given the increase in production of vaccines, DBT recognised that vaccine testing needed to be scaled up, or otherwise, there will be increased pressure on CDL and testing delays. Hence, DBT began to prepare two new testing laboratories for vaccines in two of its autonomous research institutes – the National Centre for Cell Sciences (NCCS) in Pune and the National Institute of Animal Biotechnology (NIAB) in Hyderabad. On 4th July 2021, NCCS and NIAB were officially set up as CDL for batch testing and quality control of vaccines, with the funding support of PM-CARES Funds trust (MST Notification, July 2021). This accelerated the testing process as well as made it logistically convenient for the two leading vaccine producers – BBIL for Covaxin and SII for Covishield, being located in Hyderabad and Pune, respectively.

DBT also supported the establishment of the largest network of five dedicated COVID-19 Biorepositories, composed of THSTI, Faridabad; ILS, Bhubaneshwar; inStem, Bengaluru; NCCS, Pune; and ILBS, New Delhi. Set up by August 2020 with the objective of expediting innovations in the development of diagnostics, vaccines, etc., the biorepositories were collected, stored and maintained clinical samples from the COVID-19 patients, to be accessed by researchers from the academia and industry. In addition, DBT

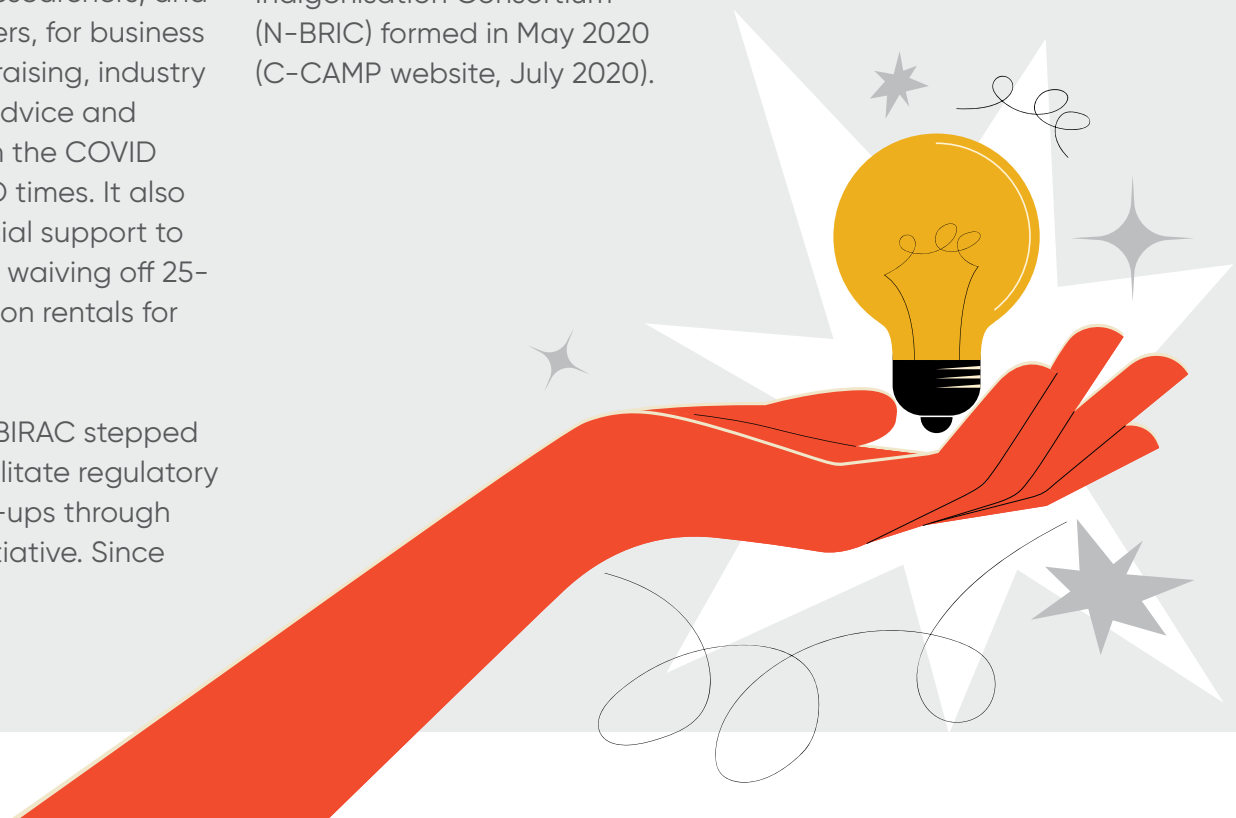
supported immunoassay labs at Interactive Research School for Health Affairs (IRSHA) Pune, Syngene International Ltd, Bengaluru and THSTI, New Delhi (MST Notification, August 2020).

Supporting Start-ups

The DBT also leveraged the private sector in the vaccine development efforts, and in the process, strengthened the spirit of Atmanirbhar Bharat. In this regard, DBT's PSU BIRAC had already been providing nurturing support for the biotech start-ups through its Incubation Centre BioNEST. During the pandemic, 50 BioNEST incubators nurtured 100+ Startup solutions for COVID-19, conducted more than 200 Webinars with an outreach of 20,000 start-ups, entrepreneurs, researchers, and other stakeholders, for business mentoring, fundraising, industry connect, legal advice and how to sustain in the COVID and post-COVID times. It also extended financial support to the start-ups by waiving off 25-100% of incubation rentals for three months.\

DBT along with BIRAC stepped up efforts to facilitate regulatory support to start-ups through its FIRST HUB initiative. Since 3rd April 2020, representatives from ICMR, CDSCO, and others joined for special weekly sessions once a week to address start-up queries on an ongoing basis. Regulatory facilitation of over 250 start-ups was also done through Facilitation of Innovation & Regulation for Start-ups and Innovators (FIRST) Hub and Regulatory Information & Facilitation Centre (RIFC) (DBT, 2021).

DBT also undertook other initiatives to incentivise and leverage indigenous innovation related to COVID-19 treatment and vaccination to combat the pandemic. Notable initiatives were the COVID-19 Research Consortium announced in March 2020 (BIRAC Website, March 2020). and the National Biomedical Resource Indigenisation Consortium (N-BRIC) formed in May 2020 (C-CAMP website, July 2020).



COVID-19 **Research Consortium**

The COVID-19 Research Consortium, launched in March 2020, solicited Request for Proposals (RFP) with a focus on diagnostics, vaccines, novel therapeutics, repurposing of drugs or any other intervention for control of COVID-19 by industry or academia or industry-academia participation (BIRAC Website, March 2020). Besides industry and academia, submissions were also opened to non-academic individuals.

BIRAC pushed towards expediting the procedure through its 'Fast Track Review Process', a provision to fund COVID solutions that are ready for immediate deployment. Further, DBT also roped in institutions like IIT Indore, Christian Medical College Vellore, Indian Institute of Chemical Technology, University of Delhi South Campus, among others, for making the provision of animal models for testing pre-clinical efficacy and make available neutralization assays (MST Notification, May 2020).

By 30th March 2020, the first phase of the call ended and 71 proposals received recommendation for funding support, and after a follow-up call, 49 proposals were recommended (MST Notification, January 2021). In the vaccine category, funding support was recommended under the NBM to seven proposals including Cadila Healthcare Ltd for a DNA Vaccine candidate, BBIL for a vaccine candidate utilizing the inactivated rabies vector platform and to SII for a Phase III human clinical trials study of recombinant BCG vaccine (VPM1002). Additionally, it was also recommended to fund the National Institute of Immunology for the development of a novel vaccine evaluation platform for SARS-CoV-2 (MST, 2020).

By May 2020, DBT and BIRAC reviewed all applications. They recommended 70 proposals of devices, diagnostics, vaccine candidates, therapeutics and other interventions for receiving financial support, including ten vaccine candidates in India. Under the Vaccine category, a total of 19 proposals by the small and the large vaccine industry and academic institutes were recommended. The NBM, Ind-CEPI, and BIRAC together worked with DBT to support the recommended proposals under the Consortium. Besides the candidates recommended after the first phase of the call, other candidates included Biological E for a Subunit Vaccine, THSTI and Gennova Biopharmaceuticals for an mRNA vaccine, Intas Biopharmaceuticals, and Seagull Biosolutions.

At the time of writing this report, nearly 15 projects by industry and public sector laboratories, for the development of vaccine candidates and associated resources, were being supported by DBT and BIRAC. Also, the seed funding was provided to early-stage candidates and candidates at advanced preclinical stages, and support was provided for the development of animal models for vaccine efficacy testing.

Additional Sources: Documents shared by DBT

The Indian SARS-CoV-2 Genomic Consortia (INSACOG) was launched on 30th December 2020. Jointly initiated by the Union Health Ministry of Health, and DBT with Council for Scientific & Industrial Research (CSIR) and ICMR

Miscellaneous

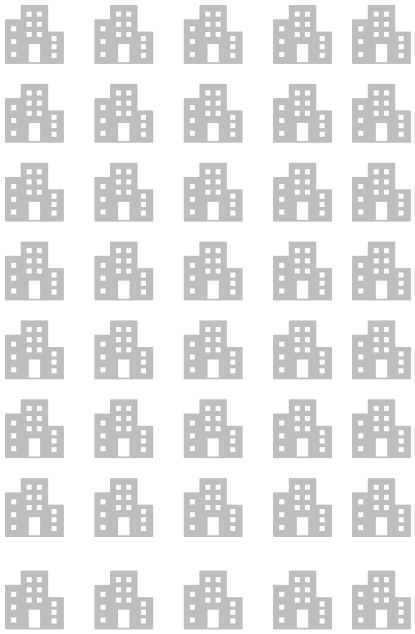
DBT's role in vaccine development did not end even by the end of 2020, as new variants of the coronavirus that was found in different parts of the world necessitated further research efforts like virus surveillance, genome sequencing and characterization, in order to understand the spread and evolution of the virus. For this purpose, the Indian SARS-CoV-2 Genomic Consortia (INSACOG) was launched on 30th December 2020. Jointly initiated by the Union Health Ministry of Health, and DBT with Council for Scientific & Industrial Research (CSIR) and ICMR, INSACOG began as a network of 10 laboratories tasked with carrying out genome sequencing of positive samples from different states, with the National Centre for Disease Control (NCDC) correlating the clinical aspects coordinating sample collection (DBT, April 2021). As the proportion of cases with variants of concern (VoC) rose exponentially during May-June 2021, INSACOG expanded to a network of 28 national laboratories on 28th June, 2021 (DBT, June 2021). Now a multi-laboratory, multi-agency, pan-India network of laboratories, INSACOG carries out whole-genome sequencing of coronavirus across the nation, thus aiding the understanding of how the virus spreads and evolves, and provide information which informs public health response. It also aims to focus on the sequencing of clinical samples to understand the disease dynamics and severity (DBT, April 2021).

Vaccine Development – Initiatives

India went ahead with two main strategic choices while going for COVID-19 vaccine development. The first choice involved going ahead with the indigenous development of new candidate vaccines, drugs and molecules. In this direction, the Drug Controller General of India (DCGI) permitted clinical testing and development of local vaccines by multiple pharmaceutical companies in India. The second strategic action involved facilitating collaboration between leading vaccine manufacturers in India and leading global COVID-19 vaccine development companies at an early-stage, so as to ensure their performance reliability based upon the trials in India, local capacity building as well as mass-manufacturing at the time of global launch.

Strategic Choice 1 – Focus on Indigenous Vaccine Development

More than



300 companies

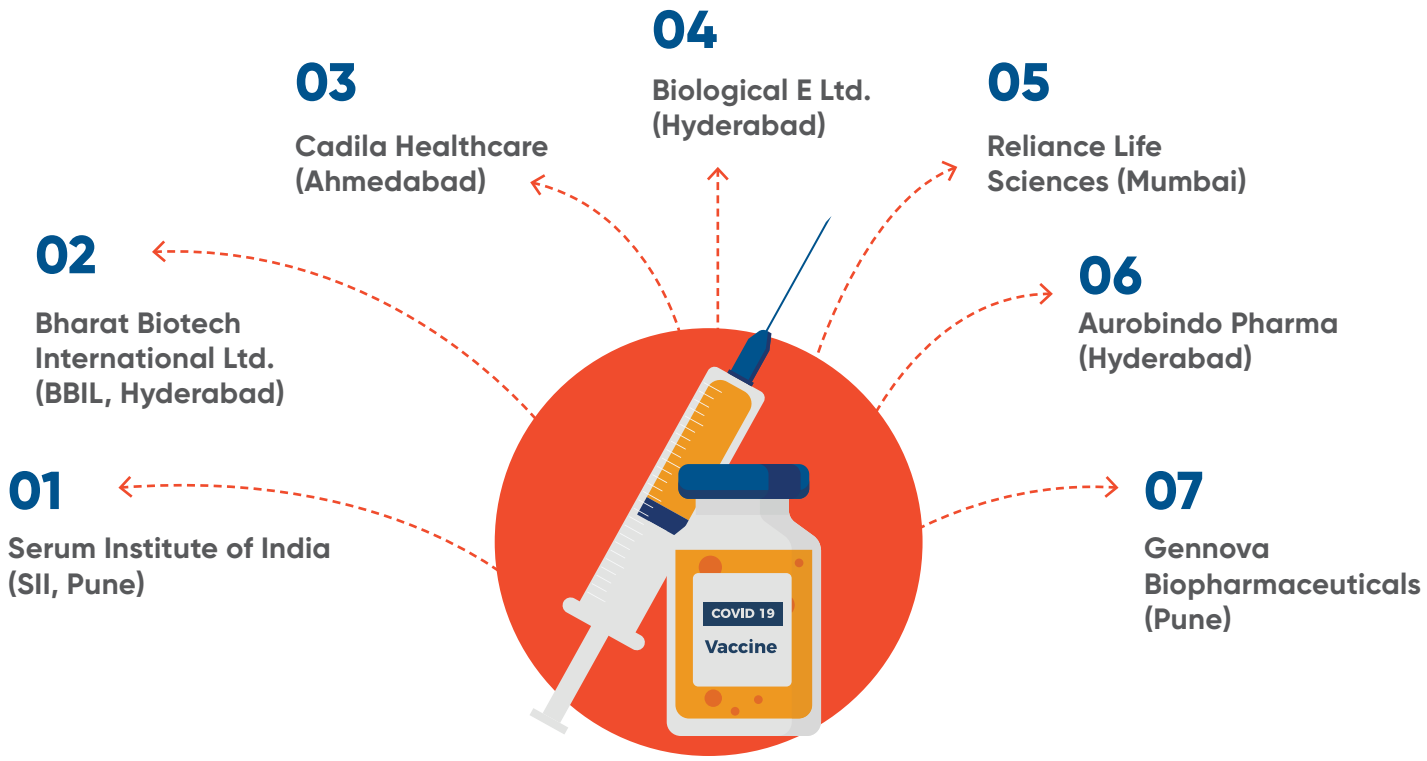
were working towards the development of COVID-19 vaccine globally in 2020.

GoI made the decision very early during the COVID-19 pandemic that it will focus on the indigenous vaccine development to tackle the COVID-19 crisis. The credit for the indigenous vaccine development initiative goes to the GoI because it made the decision well in advance during the pandemic and brought together all the key stakeholders to develop and implement the solution.

More than 300 companies were working towards the development of COVID-19 vaccine globally in 2020. In India, the vaccine development initiative led to significant collaborative efforts among the government, academic institutions, R&D institutions and pharmaceutical industry leaders. GoI tried its best to bring the best minds, as well as R&D, science and technology capabilities together for the common cause. As of 25th May, 2020 more than 30 companies and institutions started working on the COVID-19 vaccine and were in different stages of trials and development. To give a further boost to vaccine development, GoI allocated Rs 100 crores from the PM-CARES Fund towards vaccine development initiatives.

Even as leading vaccine candidates were busy with different stages of vaccine development, GoI used the vaccine development phase as another avenue for further stimulating innovation among the scientific community and launched the Drug Discovery Hackathon 2020 (DDH2020) on July 2, 2020. This was India's first-ever national initiative for supporting the drug discovery process. DDH2020 was launched as a joint endeavour by the Ministry of Human Resource Development (MHRD), Ministry of Education Innovation Cell (MIC), All India Council for Technical Education (AICTE) and Council of Scientific and Industrial Research (CSIR) with support by the Centre for Development of Advanced Computing (CDAC), MyGov as well as private players. This Hackathon invited participation from professionals, faculties, researchers and students from diverse fields. The task of the MIC and AICTE was to identify potential drug molecules through the Hackathon, while CSIR took those identified molecules forward for synthesis and laboratory testing for efficacy, toxicity, sensitivity and specificity (MST, July 2020).

By September 2020, CDSCO granted test license permission to the following seven vaccine candidate companies for the manufacture of COVID-19 vaccine, preclinical testing, examination and analysis–



In November 2020, India's push for indigenous COVID-19 vaccine development and capacity building gained greater momentum when GoI launched "Mission COVID Suraksha", an Indian COVID-19 Vaccine Development Mission, and committed Rs.900 crore for the first phase of the mission, that is, for a period of 12 months (MST, November 2020). While the DBT had been extending financial support to vaccine candidates under the NBM, the additional funding under Mission COVID Suraksha further facilitated the process. With a focus on Atmanirbhar, the Mission aimed to bring a safe, effective, convenient, and available COVID vaccine to the citizens of the country as well as the entire world, in keeping with the values of 'Vasudhaiva Kutumbakam'.

Led by DBT and implemented by a dedicated Mission Implementation Unit (MIU) at BIRAC, the Mission "COVID Suraksha" aimed at accelerating the end-to-end vaccine development process from pre-clinical development to manufacturing and regulatory facilitation for deployment. Accordingly, the funds were allocated towards accelerated product development as well as support to the development of common harmonized protocols, trainings, data management systems, regulatory submissions, internal and external quality management systems and accreditations.

At the time of the launch in November 2020, five vaccine candidates were in different stages of human trials in India, including the indigenously developed Covaxin. Under the Mission, support was extended to the five vaccine candidates in an advanced stage of development, 19 clinical trial sites, six facilities for immunogenicity assays and animal challenge models. In order to ensure that all vaccines being introduced through the Mission have preferred characteristics applicable for India, it was proposed to be achieved in two ways:

- Accelerating the production of clinical trial material, and clinical development for licensure of COVID-19 vaccine candidates
- Establishing clinical trial sites, immunoassay laboratories, central labs and suitable facilities for animal challenge studies, manufacturing facilities and other testing facilities to support COVID-19 vaccine development.

To this end, DBT published three Request for Expression of Interest (REOI) with the following focus areas:

1. **Development of Vaccine Candidate(s):**
   Herein, five proposals for the development of vaccine candidates were recommended for support.

2. **Enhancement of Capacity to Support COVID-19 Vaccine Development:**
   The purpose was to improve service facilities available to COVID-19 vaccine developers for the conduct of animal studies and immunological assays. Six projects were recommended for financial support under REOI-2, and a follow-on the call was also announced inviting REOI-2 for Enhancement of Capacity to Support COVID-19 Vaccine Development.

3. Enhancing the Capacity to Conduct Human Clinical Trials For COVID-19 Vaccine Candidates:

The mandate of the third REOI was to ensure the accessibility and availability of Good Clinical Practice (GCP) compliant clinical trial sites to vaccine developers. A total of 19 sites, including hospital and/or community settings, were identified across the country, each with trained staff, clinical trial infrastructure, a volunteer database of at least 2000 subjects, and community engagement programmes.

In addition, facility augmentation of production capacities for Covaxin was considered to support the demand for vaccine in the country. To this end, efforts were undertaken to enhance the capabilities of Bharat Biotech's own manufacturing facility such that the production of Covaxin by Bharat Biotech was increased from 1 crore per month to 10 crores per month within 4-5 months. The following public/private entities were recommended for facility augmentation for Covaxin manufacturing scale-up in India:

1. Bharat Biotech International Ltd. (BBIL)
2. Indian Immunological Ltd. (IIL)
3. Bharat Immunologicals & Biologicals Corporation Ltd. (BIBCOL)
4. Haffkine Bio-Pharmaceutical Corporation Ltd. (A Government of Maharashtra Undertaking)

In this regard, facilitation and expert advisory support was also provided by the DBT as per the needs.

Strategic Choice 2 – Go for Global Tie-ups, Local Trials and Capacity Building

Through the multi-pronged approach taken by the GoI, the Indian version of Oxford-AstraZeneca vaccine, Covishield, and indigenously developed Covaxin emerged as India's leading vaccine candidates and got emergency use approval by the Subject Expert Committee and DCGI on 3rd January 2021 (PIB Press Release, January 2021)

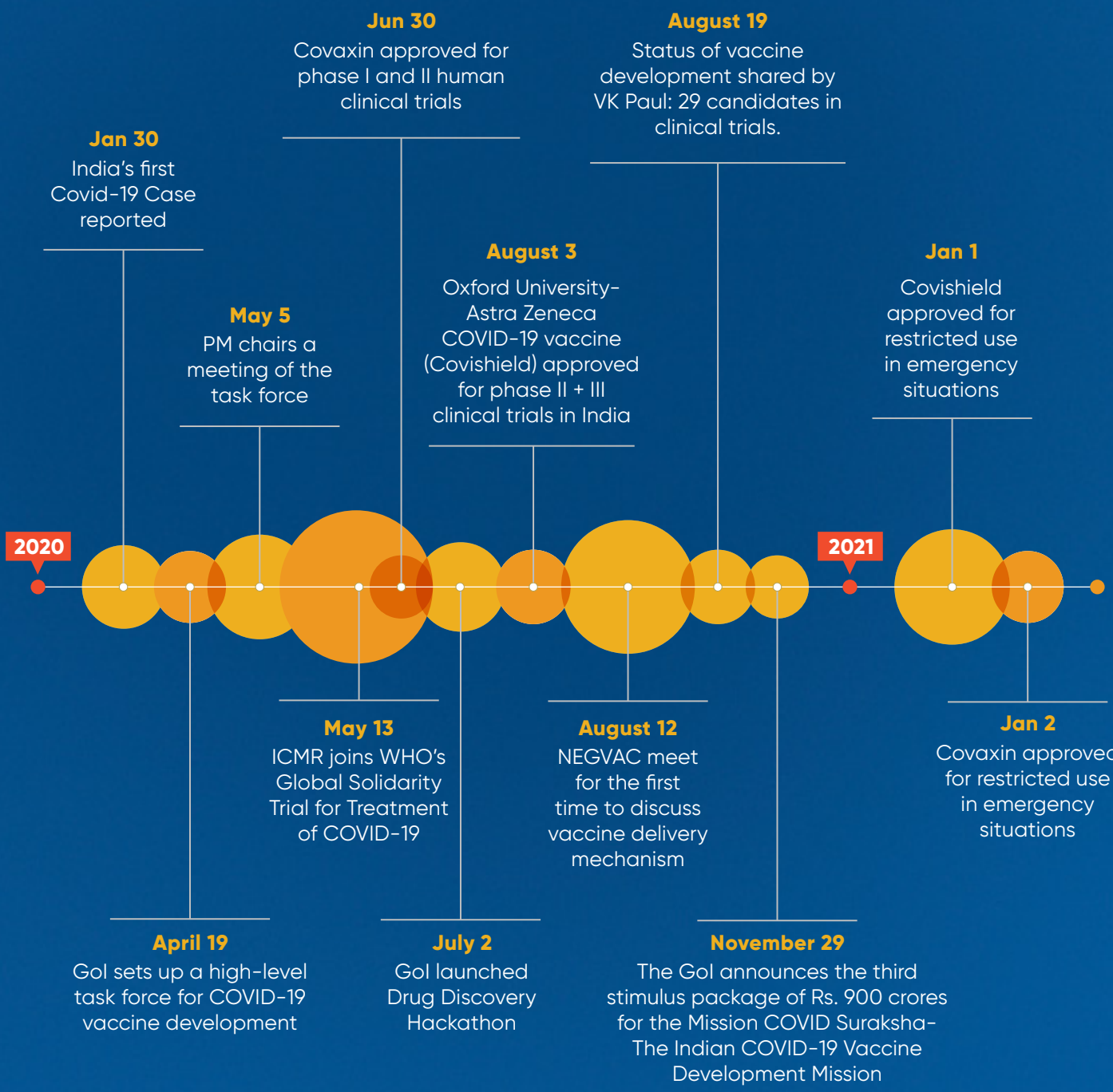
Regarding licensing deals, GoI encouraged Indian pharmaceutical companies to collaborate with the global vaccine candidates for India trials, technology transfer and mass manufacturing of vaccines in India post-global approvals and launch. At one end, this was a risk mitigation strategy by aligning with global vaccine candidates in parallel to indigenous vaccine development. At another end, early-stage tie-up gave an opportunity to test the potential vaccine in Indian geography thereby knowing the risks early as well as getting into a position of fast-track approvals by Indian authorities at the time of global launch. Serum Institute of India (SII) took the lead in this endeavour by partnering with multiple global vaccine developers like Oxford University, USA biotech firms Codagenix and Novavax, and Austria's Themis Bioscience.

Amidst all these developments, the Task Force acted as a nodal point of information and updates regarding global vaccine development progress for the GoI. The Task Force convened the proper tracking, monitoring and communication of the global vaccine development progress to the key government and private stakeholders in India. It set up the "clinical cohorts" focussing on a better understanding of coronavirus disease and its management. The Task Force, therefore, bridged the gaps between various stakeholders and coordinated the efforts of the government, academia, industry and other key organizations to facilitate not only indigenous vaccine development but also global tie-ups.

Through the multi-pronged approach taken by the GoI, the Indian version of Oxford-AstraZeneca vaccine, Covishield, and indigenously developed Covaxin emerged as India's leading vaccine candidates and got emergency use approval by the Subject Expert Committee and DCGI on 3rd January 2021 (PIB Press Release, January 2021). Covaxin also became the first indigenously produced COVID-19 vaccine candidate to get approval for phase I and II clinical trials on 30th June, 2020 merely six months after the appearance of the first corona case in the country. (h ENS Economic Bureau, June 2020)

Refer to Figure 5 for a detailed view regarding the chronology of key events, which happened during the vaccine development and access journey.

Figure 5: COVID-19 Vaccine Development in India – Chronology of Key Events



Source: Adopted from PIB releases

India's Access Strategy – Covishield and Covaxin as Frontrunners

India's access strategy during the first wave of coronavirus relied heavily on the development and launch of COVID-19 vaccines by the Serum Institute of India (SII) and Bharat Biotech India Limited (BBIL).

Covishield (SII)

After getting the approval on 3rd August 2020 (PIB release, 3rd August 2020), the institute collaborated with ICMR to conduct the Phase II/III clinical trials on

1600 voluntary participants across 15 sites in India

SII, one of the largest vaccine manufacturers globally has been the main frontrunner in ensuring the supply of COVID-19 vaccines in India. SII adopted a multi-pronged strategy of licensing, development and production setup to become battle-ready since the early days of the outbreak. This foresightedness on the part of SII is one of the primary reasons for the launch of COVID-19 in January 2021.

In April 2020, it was announced that SII had joined the Oxford vaccine project as one of the seven global institutions involved in manufacturing the vaccine (India Today Web Desk, April 2020). In June, SII entered into a licensing deal with AstraZeneca, a British pharmaceutical company, to carry out the mass-production of the vaccine in India (AstraZeneca, June 2020). It must be noted that AstraZeneca became the University of Oxford 's vaccine manufacturing and distribution partner in late April. (AstraZeneca, April 2020)

In parallel, SII also tied up with the US-based biotech firm Codagenix and Austrian biotech company Themis Bioscience on two other COVID-19 vaccine candidates. (Siddiqui, April 2020). In addition, SII's parent company, Cyrus Poonawalla Group sold its Czech Republic-based subsidiary, Praha Vaccines to Novavax in May 2020 for around USD 167 million thereby Novavax' global manufacturing capacity (Novavax, May 2020). The acquisition was beneficial for India as later in August 2020, SII and Novavax forged a licensing agreement for the development and commercialization of Novavax' COVID 19 vaccine candidate in low and middle income countries (LMIC) including India. (Novavax, August 2020)

Thus, SII diversified its approach to accessing COVID-19 vaccine, in order to ensure India was able to begin manufacturing at the earliest, depending on whichever vaccine candidate received the green light first. This strategy helped SII to finally manufacture and launch Oxford-Astrazeneca's Covishield vaccine and get approved for "restricted use" by January 2021.

As mentioned above, the development of Covishield began with SII's decision to partner with the Oxford vaccine project as one of the seven global institutions behind manufacturing the vaccine. The vaccine development began at the Oxford University by the Jenner Institute and Oxford Vaccine Group, and went for Phase-1 clinical trial on 23rd April 2020 (Prasad, April 2020). On 30th April 2020, Oxford received a major push in its endeavour when AstraZeneca announced an agreement with Oxford University to collaborate in the development, manufacturing and distribution of the potential vaccine, known as ChAdOx1 nCoV-19 globally (AstraZeneca, April 2020). In July 2020, even as phase III clinical trials continued in the UK, SII took the calculated risk and began the production of the vaccine post technology transfer from AstraZeneca/ Oxford University for Phase II and III trials in India (Prasad, July 2020). SII branded the vaccine as Covishield. After looking at the favourable results of the Phase I/II trials conducted by the Oxford University-Astra Zeneca in terms of induced antibody immune response (Folegatti, Ewer, Aley, Angus, Becker, & Belij-Rammerstorfer, 2020), SII sought DGCI's approval for conducting the Phase II+III clinical trials in India. After getting the approval on 3rd August 2020 (PIB release, 3rd August 2020), the institute collaborated with ICMR to conduct the Phase II/III clinical trials on 1600 voluntary participants across 15 sites in India (ICMR, March 2021) The trials showed encouraging results in terms of safety, immune response, immunogenicity and efficacy, and Covishield got the formal recommendation as "restricted use" in January 2021 (Sen, January 2021).

Covaxin (BBIL)

While kick-starting the vaccine development, ICMR and BBIL targeted a timeframe of 6-8 months for development, clinical trials, approvals and launch in India by the end of 2020

BBIL was identified as another vaccine candidate in India. ICMR entered into a partnership with BBIL to develop a fully indigenous COVID-19 vaccine in India (PIB release, 3rd Mar 2021). Dr Rajnikant Srivastava, ICMR's head of the Department of Research Management, Policy Planning and Communication, Delhi highlighted that ICMR decided to enter into a partnership with BBIL for indigenous COVID-19 vaccine development and manufacturing due to its expertise in vaccine development specifically how BBIL developed the vaccine for Japanese encephalitis (Chakrabarti, May 2020). ICMR kick-started the indigenous COVID-19 vaccine development initiative in March 2020 when there were less than ten active cases in India. Within two months (March – April, 2020), ICMR isolated the virus at National Institute of Virology (NIV) at Pune, cultured it, and transferred the strain to BBIL to initiate the development stage for COVID-19 vaccine (Chakrabarti, May 2020). While kick-starting the vaccine development, ICMR and BBIL targeted a timeframe of 6-8 months for development, clinical trials, approvals and launch in India by the end of 2020. In June 2020, ICMR and BBIL sought and received the fast-track approvals for conducting the Phase I and II human trials for the COVID-19 vaccine (code named as BBV152) from the Subject Expert Committee (SEC) of Drugs Controller General of India (DCGI). ICMR and BBIL selected twelve sites including the all India Institute of Medical Sciences (AIIMS), Delhi for conducting Phase I and II randomized, double-blind and placebo-controlled clinical trials for the BBV152 vaccine (DD-News, July 2020).

In Phase I, sampling involved **around 375 volunteers** with a maximum of 100 from AIIMS in the age group of 18 – 55 years and having no prior history of comorbid conditions or COVID-19.

In Phase II, sampling involved around **750 volunteers** from 12 selected sites (Saxena, July 2020). The outcomes or results of both trials showed the efficacy of the COVID-19 BBV152 vaccine. However, Phase II trials had higher immune response and induced T-cell response than Phase I due to the higher dosing interval in Phase II (4 weeks) than Phase I (2 weeks).

BBIL and ICMR decided to conduct Phase III clinical trials in November 2020.

They planned to conduct Phase III trials on 26000 volunteers pan-India (The Hindu, October 2020). To assess the efficacy of the BBV152 vaccine and to get a go-ahead for Phase III trials from DCGI, BBIL submitted the results of Phase I and Phase II trials along with the results of testing on two animal species to the SEC of DCGI (The Hindu, October 2020). BBIL presented the Phase III clinical protocol to the SEC and finally got permission for conducting Phase III trials from SEC on 20th October 2020. The Phase III trials, jointly conducted by ICMR and BBIL, were conducted across 21 sites involving a total of 25,800 individuals. The results of the trials were then evaluated by an independent data safety and monitoring board and revealed that the vaccine holds its efficacy across age groups and is effective against the variants prevalent in the country. The interim efficacy value ascertained after thorough analysis in accordance with DCGI protocol stood at 81%, which positioned Covaxin, Bharat ki Apni Vaccine, on par with global front-runner vaccines (MOHFW, 3 March 2020). Based upon the efficacy results of the in-progress Phase III trials, BBIL COVID-19 vaccine BBV152 got the formal recommendation as "restricted use" on 2nd January 2021 (Sen, January 2021).

Role of ICMR **in Covaxin development**

The journey of developing Covaxin began with the public-private partnership initiated between ICMR and Bharat Biotech International Limited (BBIL), announced on May 9, 2020. However, it can also be said that the process effectively began as far back as on 9th March 2020, when ICMR's National Institute of Virology (NIV) Pune isolated the SARS-CoV-2 virus, making India the fifth country in the world to achieve the feat. This milestone marked India's first step towards the development of drugs, vaccines, rapid diagnostic kits, monoclonals and so on. While there are other means to do the same, ICMR chose to isolate and culture the live virus, a process that is considered the most ideal, albeit more time-taking and requiring stricter safety protocols than alternatives like the pseudo virus.

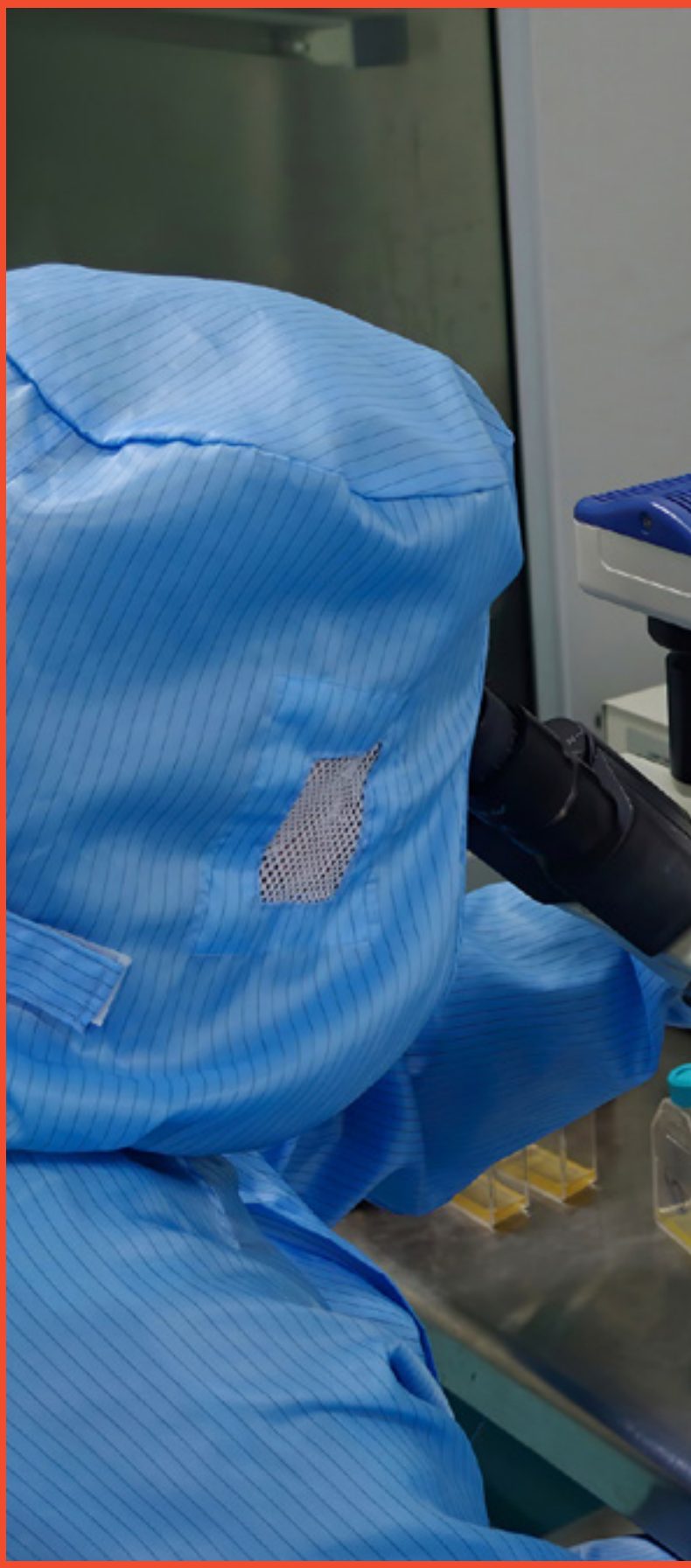
The process of vaccine development using live virus involves inactivating the live virus using chemicals, heat or radiation, so that the virus cannot multiply anymore. However,

the pathogen is still intact, which results in the immune system recognizing it and producing an immune response. The vaccine so produced is called an inactivated vaccine. Since its development poses greater risk of infecting laboratory staff, manufacturers borrowing the live virus strain must have at least a Biosafety Level 3 (BSL3) facility, and have to adhere to strict safety protocols based on international norms involving stringent documentation.

Fortunately, before the pandemic had begun, BBIL had been planning to produce Inactivated Polio Vaccine (IPV), and had therefore built a BSL3 facility for the same. ICMR, being the focal point for promoting IPV manufacture and validating facilities for IPV, had already inspected their BSL3 facility for appropriateness. So, when BBIL approached ICMR for borrowing the SARS-CoV-2 virus strain, the partnership took off without much delay.

BBIL already possessed the ICMR validation and certification, and immediately got to repurposing the same facility for making the COVID-19 vaccine. After all the necessary paper work and with due diligence, ICMR gave the virus to BBIL along with several protocols on how to grow the virus and inactivate it.

In this partnership, the intellectual property rights for the use of Covaxin are shared between both organizations. The partnership involved 12 activities, wherein ICMR shared its scientific wisdom in the form of protocols and SOPs with BBIL as part of technology transfer,



and also funded the Phase III clinical trials. On the other hand, BBIL funded five activities including vaccine development, Phase I and II trials, preclinical studies, and more.

All in all, this partnership saw the deep involvement of both the parties at every step. In the early stages of development when BBIL were able to make their own vaccine candidate, the process progressed with them sending all the material to NIV Pune for characterization. The institute ran several tests to check whether the virus was properly inactivated or not, and ensure that it had its surfaces intact and looked very much in appearance like the live SARS-CoV-2, so as to confirm its immunogenic potential. Thereafter, based on NIV's inputs, the manufacturer made several tweaks to the candidate, and eventually made a successful candidate.

For every vaccine, it is imperative to do preclinical studies in small animals and then large animals. Once the vaccine was characterized appropriately, BBIL conducted studies on small animals like rabbits and rats at their own facility, and sent samples to NIV for characterization and titration of the antibody responses, and to detect which vaccine would serve better as a vaccine candidate. BBIL used around five to six different formulations, and based on the characterization studies, three candidates were selected for further studies. These candidates were then again given to NIV, who conducted studies on hamsters, and later on non-human primates or monkeys. This was done mainly to build confidence in the vaccine and do as many preclinical characterizations as possible.

The study on monkeys was among the most challenging parts of Covaxin's development journey, owing to the stringent norms related to the use of animals for experimentation. Nevertheless, with the support and cooperation of the GoI, the Maharashtra Government and forest authorities, ICMR was able to go ahead with the study. It began with catching a monkey from the forest with the help of NGOs and forest officials, and following protocols requiring them to be quarantined and subjected to various tests in order to rule out tuberculosis and other viral and respiratory diseases. The study commenced after all such necessary tests were undertaken. ICMR/NIV injected the monkeys with three doses of the vaccines and studied their antibody response. Then, the monkeys were challenged with live the SARS-CoV-2 virus through the nasal route. To ensure if the vaccines work or not, the scientists checked for any virus present in their bodies after the autopsy. Two effective vaccine formulations emerged from these studies – 3 microgram virus plus adjuvant formulation and 6 microgram virus plus adjuvant formulation – which had showed fairly well results in the hamsters as well. The vaccinated monkeys did not show any detectable virus in their lungs, which is the main site for coronavirus multiplication, whereas the non-vaccinated group showed huge quantities of the virus in the lungs. That is where the vaccine really showed a promise in terms of viral clearance and protection from multiplication of the virus in the key target organs.

All of the above studies were conducted between July - August 2020, and the vaccines were able to complete Phase I and II clinical trials and proceed to Phase III by November. The completion of the pre-clinical studies and clinical trials in such a short period is unprecedented, and made possible because of the reformed regulatory pathways that allowed parallel animal and human trials. Earlier, stages of vaccine development took place one after the other. For instance, after a trial would be conducted, the data would be then compiled and submitted to the DCGI, and thereafter, the next trial would only be conducted after the DCGI gives approval for the next step. In this pandemic, the DCGI has had an innovative mechanism, wherein animal studies and human trials can be done in parallel once the safety of the vaccine candidate is established. This expedited the development and launch of Covaxin. Additionally, the ICMR also managed to publish the relevant data in peer-reviewed international journals, which helped build confidence around these vaccines.

Another reason for the shortened timeline for vaccine development is that every vaccine producer started moving towards well-characterized platforms. Earlier, when vaccines used to be prepared, if a new platform was being used for the vaccine candidate, a detailed characterisation of that particular platform was imperative. Today, the entire world has used already well-characterized platforms and they had already been producing some vaccines using those platforms. Due to these accelerated processes, Covaxin was finally approved for Restricted Use in Emergency Situations on 2nd January.

However, the role of ICMR didn't end with the development of Covaxin. Once the vaccine was rolled out, various strains of SARS-CoV-2 were reported, so it again fell onto ICMR to isolate and culture all these variant strains, and test whether Covaxin works against them or not, a task ICMR efficiently executed. In fact, by isolating the UK-variant in early January, ICMR led India to become the first country to report successful isolation and culture of of the UK-variant of SARS-CoV-2. The studies

found that the neutralisation capacity of the antibodies of vaccinated individuals (vaccinated by Covaxin) was decreased in some cases, but was still good enough to combat infections arising out of the variants. The ICMR has published most of these results, and has also ventured towards working with the Serum Institute by helping them in characterizing the response of Covishield for variant strains as well.

With the onset of multiple variants of COVID-19 infecting people around the world, ICMR moved towards conducting vaccine effectiveness studies and studies capturing vaccine breakthroughs. For the former, it started gathering effectiveness data in real-life settings, and those studies were rolled out along with the programmatic introduction of the vaccines. One key insight, which emerged out of ICMR's research is that the vaccines are actually disease-modifying vaccines, which essentially cannot prevent infection, but reinfection after vaccination is at least mild in nature. This was also confirmed by reports from healthcare facilities, which have found that only a small fraction of vaccinated patients require hospitalisation.

Another challenge that emerged after the roll-out of Covaxin involved scaling up its manufacturing process. Being an inactivated vaccine, Covaxin's requirement of a BSL3 facility had been a major impediment in the way of scaling up. At the time of filing of this report, only two vaccine manufacturers have the BSL3 facility besides BBIL, namely Panacea Biotech and Zydus Cadilla. Even the biggest vaccine manufacturer, SII did not own a BSL3 facility. Besides, BSL3 facilities need to be regularly audited to ensure all safety protocols are being followed, which includes 25-30 criteria for assessment. Hence, the issue was not only the lack of BSL3 facility but also the maintenance of such a facility in itself. Besides that, vaccine makers attempting to produce Covaxin also need the technology and skilled personnel required to inactivate the virus to prevent its multiplication. If the facility is not well-equipped to handle bulk virus culture, it poses a risk of infection for those dealing with the virus.

While challenges abound in the near future, given the trajectory of the pandemic remain unpredictable, the role of ICMR in various stages of COVID-19 vaccination development cannot be denied.

Source: Insights based on conversation with Dr. Nivedita Gupta, ICMR (25 May 2021)

Figure 6: Covaxin Development Timelines (2020-21)

Covaxin Development Timeline 2020-2021

India enters the global race of COVID- 19 vaccine development

11 March 2020

Experiments conducted on small animals showcase promising results establishing the efficiency of Covaxin

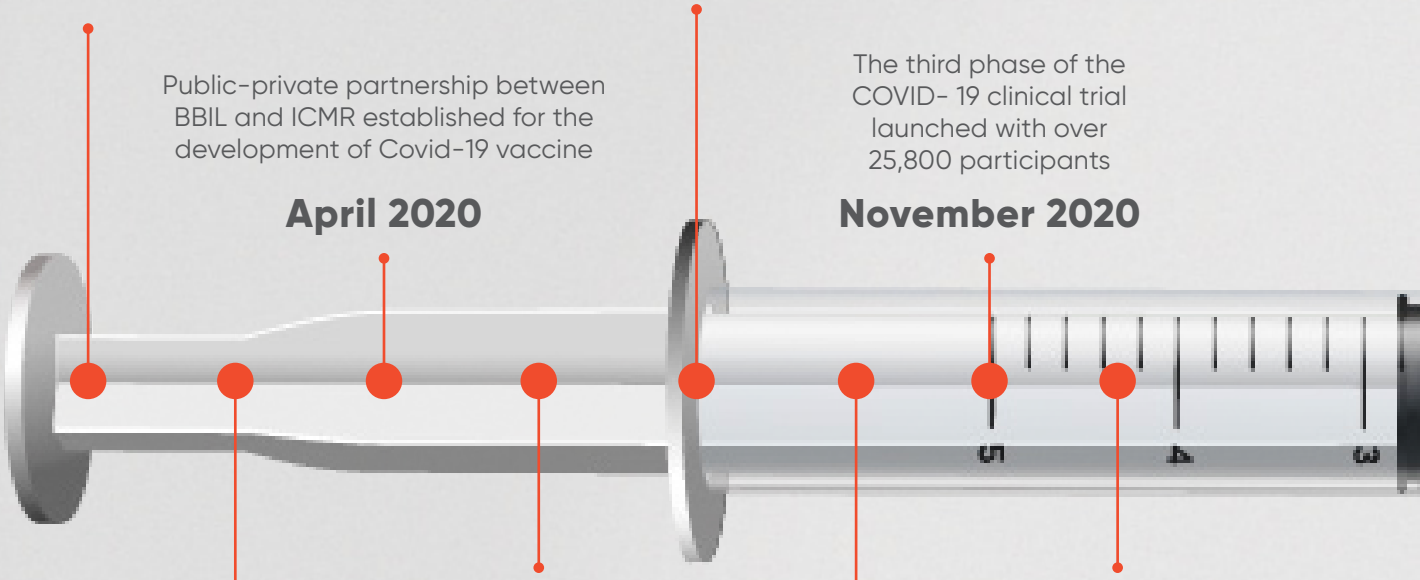
June-August 2020

Public-private partnership between BBIL and ICMR established for the development of Covid-19 vaccine

April 2020

The third phase of the COVID- 19 clinical trial launched with over 25,800 participants

November 2020



May 2020

Transfer of the isolated virus strain to BBIL and subsequent characterization of the vaccine development by BBIL through in-vitro experiments and electron microscopy studies

3 January 2021

Covaxin approved for restricted use in emergency situations by Drugs Controller General of India

13 March 2020

Successful isolation of SARS-CoV-2 virus achieved by ICMR, making India the 5th country in the world to accomplish this task

July-October 2020

Trials 1 and 2, involving 755 participants conducted. The results highlighted high safety with conversion rates of 98.3% and 81.1% respectively on days 56 and 104 respectively.

Phase 1 of COVID - 19 vaccine administration initiated. Administration of vaccine to healthcare and frontline workers

16 January 2021

Bharat Biotech announced the start of phase IV trials to evaluate the vaccine's real-world effectiveness

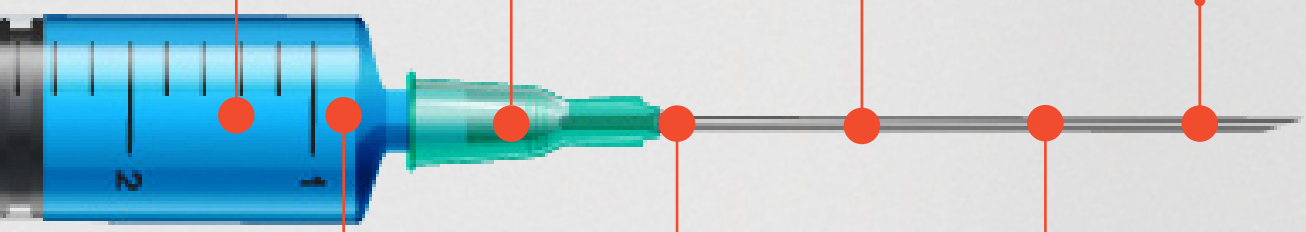
June 2021

Covaxin received EUA in Mexico, Nepal, Philippines, Iran, Paraguay, Guatemala, Nicaragua, Guyana, Venezuela, Botswana, Zimbabwe

19 April 2021

Bharat Biotech's Covaxin got approved for usage on children between 2 to 18 years of age.

12 October 2021



May 2021

Drugs Controller General of India (DCGI) approved clinical trials in the age group of 2 to 18 years

27 January 2021

Covaxin's efficiency of neutralizing UK variant established and published in Journal Travel Medicine

June 2021

Covaxin found out to be effective in neutralizing the Delta and Beta variants

Source: Adapted from MoHFW Notification (3 March 2021)

Expanding the Portfolio of COVID-19 Vaccine Manufacturers

On 12th April 2021, DCGI issued EUA to Sputnik V as third vaccine to be administered in India from May 2021 onwards, alongside Covaxin and Covishield (BBC News, Apr 2021; Kar, May 2021).

India started its vaccination drive with the EUA given to Covishield (AstraZeneca's vaccine manufactured by SII) and Covaxin (manufactured by Bharat Biotech International Limited) by the National Regulator (DCGI) on 2nd and 3rd of January 2021 respectively (BBC News, Apr 2021; MoHFW FAQs, May 2021; MoHFW Notification, 13th April 2021). As a result of EUA given to Covishield and Covaxin, India started its vaccination program on 16th January 2021 using a phase-wise approach.

In Phase-I, GoI rolled out the vaccination drive for the priority group comprising healthcare and frontline workers (doctors, nurses, param-medical and support staff) in India from 16th January 2021 (Kumar, May 2021). Subsequent planning was done to follow Phase-I by Phase-II (elderly and senior citizens having age of 45 years and above) and Phase-III (all individuals having age of 18+ years). Considering the target of vaccinating around one billion Indians with two doses each by May 2021, GoI planned the rapid expansion of the portfolio of approved vaccines beyond Covaxin and Covishield.

During Feb-Mar 2021, MoHFW started evaluating the other key vaccine candidates as well as vaccine manufacturers globally for granting EUA for supplying vaccine in India. On 12th April 2021, DCGI issued EUA to Sputnik V as third vaccine to be administered in India from May 2021 onwards, alongside Covaxin and Covishield (BBC News, Apr 2021; Kar, May 2021). Sputnik V has been developed in Russia by Gamaleya Research Institute of Epidemiology and Microbiology and will be manufactured in India by Dr. Reddy's Laboratories as a Russian Direct Investment Fund's (RDIF) Indian partner. (Parashar, May 2021). This is expected to ramp up the supply of vaccine to meet the demand of Phase III and more during May – December 2021.

According to Government estimates, India is expected to exceed the supply of two billion vaccine doses by December 2021 (Ghosh, May 2021). The scale of two billion vaccine doses will be a combination of eight COVID-19 vaccines out of which five will be Made in India.

Dr. V K Paul, NITI Aayog (Health) member said, "India is hoping to produce at least two billion vaccine doses against COVID-19 by the end of this year" (Ghosh, May 2021). Dr. Paul said that besides Covishield, Covaxin, and Sputnik V, India is expected to grant EUA to five more vaccines out of which four will be Made in India (Ghosh, May 2021). The quick summary of these vaccines in the pipeline and expected production volumes by Dec 2021 are highlighted in Table 4 below.

Table 4: COVID-19 Vaccines – Expected Supply by Dec 2021

Vaccine	Country of Origin	Developed By & Manufactured in India by	Production/ Availability (millions) (Aug-Dec 2021)	Type (Technology)	Remarks / Status
Covishield	USA/ Sweden	Univ. of Oxford, CEPI, SII	750	Adenovirus Vector	EUA Authorization in India on 1st January 2021
Covaxin (BBV152)	India	BBIL, ICMR	550	Inactivated SARS-CoV-2 (vero cells)	EUA Authorization in India on 2nd January 2021
Bio E Sub Unit Vaccine (BECOV2D)	India, US	Biological E. Limited	300	Subunit (using an antigen)	Phase III trials in progress (1,268) Apr 2021 – Aug 2021
Zydus Cadilla DNA Vaccine (ZyCOV-D)	India	Cadila Healthcare, BIRAC	50	DNA (plasmid expressing SARS-CoV-2 S protein)	Phase III trial in progress (28,216). Randomised, blind, placebo-controlled trial. Jan–May 2021, India. Three dosage vaccine to be given via needle-free technology
SII – Novavax	USA	Novovax, CEPI, SII	200	Subunit (using protein)	Phase III trial globally (45,000) including India (Till Jul-Aug 2021)
BB Nasal Vaccine (BBV154)	India	BBIL	100	Adenovirus Vector (intranasal)	Phase I trial (175) in March 2021. Single shot & needle free
Gennova mRNA Vaccine (HGC019)	India, USA	Gennova Biopharma, HDT Biotech Corp.	60	RNA	Phase I trial in progress (120)
Sputnik V Vaccine	Russia	Gamaleya Rsch Inst., Dr. Reddy Labs	156	Adenovirus Vector (Ad5, Ad26)	EUA Authorization in India on 12 April 2021
TOTAL			**2166**		

Source: ClinicalTrials (February 2021); Ghosh (May 2021); Holder (May 2021); India Today Web Desk (March 2021); Mahalingam & Taylor (Sep 2020); Pandey (April 2021); PTI (December 2020); PTI (January 2021); Raghavan P (December 2020)

06

COVID-19 Vaccine Delivery and Roll Out Planning

After the successful development of vaccines and approval granted for their distribution, the next step was formulating an end-to-end delivery plan and strategy. Ensuring a fair and equitable distribution was a key concern, given India's huge population size, limited manufacturing capacity, cold storage infrastructure and other supply chain constraints. Hence, there was a humongous need to review and formulate the extensive operational guidelines to create awareness, confidence and on-ground implementation of vaccination drive. While looking at this requirement, there were complex multi-dimensional challenges in front of the Government, which needed to be tackled for the success of vaccination drive in a country having a heterogeneous population of more than 1.39 billion people.

Following were the key questions before the GoI in December 2020 while going for the launch of one of the largest vaccination drives in India. First, how will the Government bring out the

systemic behavioural change orientation among the mass population having doubts and confusion regarding the Go-No Go for vaccine inoculation? Second, how does the Government ensure resource sufficiency and capacity building required for pan-India vaccine administration? Third, how does the Government ensure ease of access, verification of credentials, advance booking of slots, date and time notification as well as post-inoculation tracking of the people who want to get or have been vaccinated? Fourth, what will be the vaccine administration strategy in terms of the big-bang approach making it open to all irrespective of the age groups or occupation or making it phase-wise on the basis of occupation, age group and vulnerability? Further, whether Government will go all along with Centre-directed approach or if it would involve state and district level delegation? Fifth, how will the Government align with multiple stakeholders for tackling the challenge of logistics and cold-chain management especially when the vaccines need to be delivered and stored across villages pan-India in an extreme temperature-controlled setting. The majority of the COVID-19 vaccines need to be stored at a consistent temperature of 2 – 8 degrees centigrade and even less. Sixth, how will the Government ensure minimization of COVID-19 vaccine wastage especially when demand will be much more than supply? According to the data shared by MoHFW in response to the Right to Information (RTI) query, India has wasted 4.6 million doses since the launch of the vaccination drive on 16th January 2021 till 20th April 2021 (Gill, April 2021). These dosages could have vaccinated all the people of a city like Chandigarh four times.

Considering all these challenges for mass vaccination, GoI decided to adopt a multi-pronged strategy comprising the following three strategic choices. The first choice involved setting up the NEGVAC committee to oversee the vaccine roll-out strategy with the participation of key stakeholders from all major departments. This was done to ensure quick decision-making and collective efforts towards setting up the priorities and action plan without any inter-organizational conflicts. The second choice involved setting up the comprehensive operational guidelines to address the challenges related to resource sufficiency, vaccination booking, administration approach, logistics and cold chain management, and minimizing vaccine wastage. The third choice involved designing the comprehensive communication guidelines to bring out the systemic behaviour change orientation among the masses towards the benefits of vaccination as well as to keep all the stakeholders and partners aligned with the timely exchange of information on real-time basis.

In conclusion, India's confrontation with the COVID-19 pandemic showcased India's true research capabilities. The display of unity among people, which is essentially a character defining trait of the nation, highlighted how the citizens of the country can come together for a common cause in the face of adversity. Undeterred by the country-specific challenges and the pandemic-related challenges faced during the vaccine development and delivery initiatives, GoI's steadfast resolution and resilience enabled it to assemble key stakeholders and resources against time constraints and carry out the world's largest vaccination drive. GoI emphasis on a collaborative multi-partner approach accompanied by a detailed yet versatile strategy facilitated in the attainment of the vaccination initiatives success across country, including the remotest of regions. The obstacles faced along the journey made way for greater learnings and opportunities, which further improved the drive. Inarguably, the vaccination drive continues to evolve and improve over time.

07 Role of Leadership

Looking at the global impact of the COVID-19 pandemic, it was felt that developing countries like India will face the devastating effect due to the rapid spread of coronavirus. After all, India has been among the world's most populous countries having fewer resources in terms of healthcare infrastructure, skilled healthcare professionals, as well as having import dependency on other nations to meet the critical resource requirements during the pandemic situation. Negating all such assumptions, India stood out as an exemplary model in the fight against the pandemic. India's success in effectively fighting and managing the COVID-19 virus can be attributed to the multiple systemic interventions undertaken at the leadership level during the COVID-19 fightback.

Following initiatives taken by the GoI highlight the essentiality of effective leadership and its role in the success of transformative initiatives during the crisis situation. First, the GoI pushed the dual approach for vaccine readiness comprising a focus on indigenous vaccine development as well as early collaboration with global vaccine development companies for readiness and access. This reflects the clear decision-making capability of the Government during the crisis. To enable the indigenous development of the COVID-19 vaccine, Indian Government launched "Mission COVID Suraksha" and committed significant research and financial support to the potential vaccine developers in India. Second, the Indian Government brought together all the key stakeholders (Government institutions, private enterprises, individuals, research institutions, policy makers, development institutions etc.) to facilitate the fast-track development and testing of indigenous vaccine for COVID-19. This highlights the collaborative mindset and can-do attitude of the Government in a challenging scenario. The push for a collaborative approach with the engagement of diverse stakeholders on a 24*7 basis gave a significant push to the vaccine development project. In its quest for developing a "Made in India" vaccine, the GoI put great emphasis on bringing the best minds and R&D, science and technology capabilities together for a common purpose. Third, the Indian Government pushed for the early planning and capacity building to launch the vaccine administration as soon vaccine was developed, tested and approved for launch. The Government knew very well that vaccine administration will be a huge challenge considering the social, demographic and geographic landscape of India. So, it pushed for the early preparation and readiness during the vaccine development phase itself for vaccine administration. This highlights the maturity and process orientation aspect of the Government during the crisis. Multiple dynamic initiatives were taken in this direction to ensure the readiness in terms of skilled resources for vaccination, technology platform for registration and tracking, logistics infrastructure, and communication strategy. GoI set a leadership example by taking a double-barrelled approach to vaccine development characterized by the production of 'Covishield', the vaccine developed by Oxford-AstraZeneca in collaboration with Serum Institute of India and 'Covaxin', the vaccine indigenously developed by Bharat Biotech. India, in its approach to vaccine development, has set a precedent by advocating for regional cooperation and later on being a frontrunner in vaccine diplomacy. Such initiatives on behalf of the Indian Government have made it quite evident that under the able administration of PM Modi, India is capable of undertaking action-oriented approaches to problem-solving on a local as well as global scale. Under the pragmatic leadership of PM Modi, India has emerged as robust and all the more resilient from the COVID-19 adversity.

CONCLUSION

In conclusion, India's COVID-19 vaccine development journey leaves behind an exemplary model of resilience showcasing the capabilities of a developing country in the face of adversity of a lifetime, i.e. the COVID-19 pandemic. As the COVID-19 pandemic unfolded, confounding countries across the globe, developing countries, including India, faced a massive challenge of survival against all odds. India suffered from a myriad of challenges, for instance, weak healthcare infrastructure, understaffing of skilled healthcare professionals, and inability to import critical healthcare resources due to global lockdowns and import restrictions by other countries. Such challenges made the Indian population all the more vulnerable to the COVID-19 pandemic.

Amidst such predicaments, how India fought against the pandemic, subsequently emerging as a more robust, self-sustaining and resilient nation only enduring minimal unavoidable impact, fabricates an excellent learning narrative for handling crises of similar nature in the years to come. Between January-December of 2020, GoI adopted a dual approach of pushing indigenous COVID-19 vaccine development in addition to facilitating global partnerships with leading vaccine developers. Thusly, GoI created an enabling ecosystem by engaging all the key stakeholders in the vaccine development and access process. By January 2021, India had become one of the leading nations, having access to not one but two vaccines. One of the two being Covaxin, which was "Made in India". Synchronically, India developed the vaccine administration guidelines, capacity building and infrastructure. The amalgamation of the aforementioned efforts on behalf of all stakeholders involved enabled India to launch world's largest vaccination drive on the 16th of January 2021, henceforth creating history. To put it concisely, India's COVID-19 journey is a reflection of India's research capabilities, skilled manpower, willingness all citizens to come together for a common cause, never-say-never attitude and exceptional leadership.

08 Annexures

Annexure 1: Different Vaccine development Platforms

Technology Type	Tradition/ New Platform	Overview	Vaccines in Use
Inactivated vaccine	Traditional	Involves inactivated pathogens (virus or bacteria) that cannot replicate or multiply. Pathogens are inactivated by making use of chemicals like formalin.	**Major non-COVID Vaccines:** Polio, Rabies, Influenza, Cholera **COVID-19 Vaccines:** Covaxin (India), Sinovac (China), Sinopharm (China), Sinopharm-Wuhan (China), CoronaVac (China), CoviVac (Russia), QazVac (Kazakhstan)
Live-attenuated virus vaccine	Traditional	Generated by passaging in cell culture until it loses its pathogenic properties. In this vaccine, pathogen is weakened so as not to cause diseases but build immune response.	**Major non-COVID Vaccines:** Polio, Measles, Influenza, Rotavirus, BCG **COVID-19 Vaccines:** None yet
Subunit vaccine including proteins or virus like particle	Traditional	Involves part of the organism including protein or virus-like particles that is required to induce the immune response.	**Major non-COVID Vaccines:** Hepatitis B, HPV, Tetanus, Diphtheria, Pneumococcal vaccines COVID-19 **Vaccines:** Novavax (USA), CIBG-66 – ABDALA (Cuba), EpiVacCorona (Russia), RBD-Dimer (China)
Viral- vectored vaccine	New	Making use of non-pathogenic virus as a carrier of the gene sequence for a protein. In viral-vectored vaccines, virus is used as a vehicle to transport the target antigen gene into human cells thereby stimulating an immune response.	**Major non-COVID Vaccines:** None **COVID-19 Vaccines:** Oxford–AstraZeneca (UK, Sweden), Sputnik V (Russia), Johnson & Johnson (USA, The Netherlands), Convidecia (China)

Technology Type	Tradition/ New Platform	Overview	Vaccines in Use
mRNA vaccine	New	In this technology, messenger RNA is enclosed in fatty nanoparticles and is used as a carrier to transport genetic sequence for the protein (spike protein of SAR-CoV-2).	**Major non-COVID Vaccines:** None **COVID-19 Vaccines:** Pfizer–BioNTech (Germany, USA), Moderna (USA)
DNA vaccine	New	In this technology under research, gene sequence for a protein is encoded on a DNA molecule.	**Major non-COVID Vaccines:** None **COVID-19 Vaccines:** No licensed vaccine for humans yet. In trial for horses.

Sources: WHO (Jan, 2021); U.S. Department of Health and Human Services (2021); Craven (June, 2021)

09 References

1. AstraZeneca (30 April 2020). AstraZeneca and Oxford University announce landmark agreement for COVID-19 vaccine. https://www.astrazeneca.com/media-centre/press-releases/2020/astrazeneca-and-oxford-university-announce-landmark-agreement-for-COVID-19-vaccine.html (last accessed 17 June 2021)

2. AstraZeneca (4 June 2020). AstraZeneca takes next steps towards broad and equitable access to Oxford University's potential COVID-19 vaccine. https://www.astrazeneca.com/media-centre/articles/2020/astrazeneca-takes-next-steps-towards-broad-and-equitable-access-to-oxford-universitys-potential-COVID-19-vaccine.html (last accessed 17 June 2021)

3. BBC News (14 April 2021). Sputnik V, Covishield, Covaxin: What we know about India's COVID-19 vaccines. https://www.bbc.com/news/world-asia-india-55748124 (last accessed 5 May 2021)

4. Bhaduri, A (18 May 2021). Covaxin trials in children between 2 and 18 years to begin in 10-12 days, says Niti Aayog member. Hindustan Times.

5. Bharat Biotech. (24 January 2018). World Health Organization Grants Prequalification to Bharat Biotech's rotavirus vaccine, ROTAVAC. https://www.bharatbiotech.com/images/press/WHO-Grants-Prequalification-to-Bharat-Biotech's-rotavirus-vaccine-ROTAVAC-Jan-2018.pdf

6. Bharadwaj, S (20 April 2021). Covid-19: Bharat Biotech ramps up Covaxin capacity to 700 million doses per annum. Times of India.

7. BIRAC Website (19 March 2020). DBT and BIRAC announce COVID-19 Research Consortium. https://birac.nic.in/cfp_view.php?id=45&scheme_type=32 (last accessed 19 May 2021)

8. Brahma, D., Chakraborty, S., and Menokee, A. (2 Apr 2020). The early days of a global pandemic: A timeline of COVID-19 spread and government interventions. https://www.brookings.edu/2020/04/02/the-early-days-of-a-global-pandemic-a-timeline-of-COVID-19-spread-and-government-interventions/ (last accessed 17 June 2021)

9. Broom, D. (2 June 2020). 5 charts that tell the story of vaccines today. World Economic Forum. https://www.weforum.org/agenda/2020/06/vaccine-development-barriers-coronavirus/ (last accessed 12 May 2021)

10. Buchholz, K. (11 May 2020). The Most Widespread Vaccines in the World. Statistica. https://www.statista.com/chart/21644/most-widespread-vaccines-globally/#:~:text=According%20to%20immunization%20coverage%20data,were%20the%20next%20most%20common (last accessed 12 May 2021)

11. C-CAMP Website (9 July 2020). C-CAMP led National Biomedical Resources Indigenization Consortium is paving the way for India's self-reliance. http://www.ccamp.res.in/node/1406 (last accessed 21 May 2021).

12. Chakrabarti, A. (10 May 2020). India to develop 'fully indigenous' COVID vaccine as ICMR partners with Bharat Biotech. The Print. https://theprint.in/health/india-to-develop-fully-indigenous-COVID-vaccine-as-icmr-partners-with-bharat-biotech/418180/ (last accessed 19 May 2021)

13. ClinicalTrials (12 February 2021). Safety and Immunogenicity of an Intranasal SARS-CoV-2 Vaccine (BBV154) for COVID-19. ClinicalTrials.gov. United States National Library of Medicine (last accessed 24 May 2021).

14. CNBC TV18 (10 June 2021). Bharat Biotech plans Covaxin Phase 4 trials, says will meet 'every scientific standard (last accessed 3 July 2021)

15. Co-Win (5 May 2021). https://dashboard.cowin.gov.in/ (last accessed 5 May 2021)

16. Craven, J. (17 June 2021). COVID-19 vaccine tracker. Regulatory Affairs Professionals Society https://www.raps.org/news-and-articles/news-articles/2020/3/COVID-19-vaccine-tracker (last accessed 17 June 2021).

17. DBT (21 April 2021). Indian SARS-CoV-2 Genome Sequencing Consortia (INSACOG). DBT India. https://dbtindia.gov.in/sites/default/files/Note%20on%20INSACOG%20Data%20and%20Mutants%2021-04-2021.pdf

18. DBT (2021). Annual Report 2021-2021. https://dbtindia.gov.in/sites/default/files/Final%20English%20Annual%20Report%202021.pdf

19. DBT (28 June 2021). INSACOG Bulletin. DBT India. https://dbtindia.gov.in/sites/default/files/INSACOG%20WEEKLY%20BULLETIN%20June%2030.pdf

20. DD-News (25 July 2020). Human clinical trials of potential COVID-19 vaccine 'Covaxin' started at AIIMS. http://ddnews.gov.in/health/human-clinical-trials-potential-COVID-19-vaccine-%E2%80%98Covaxin%E2%80%99-started-aiims (last accessed 19 May 2021)

21. Deo, S., Manurkar, S.,Krishnan, S., & Franz, C. (10 July 2020). COVID19 Vaccine: Development, Access and Distribution in the Indian Context. Observer Research Foundation. https://www.orfonline.org/research/COVID19-vaccine-development-access-and-distribution-in-the-indian-context-69538/ (last accessed 16 May 2021).

22. DoBT (20 March 2020). Rapid Response Regulatory Framework for COVID-19 to deal with applications for development of vaccines, diagnostics, prophylactics and therapeutics. Department of Biotechnology. https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=NTc4Mw== (last accessed 19 May 2021)

23. DoP Annual Report (2020). Department of Pharmaceuticals – Annual Report 2019-20. https://pharmaceuticals.gov.in/sites/default/files/Annual%20Report%202019-20.pdf (last accessed 9 May 2021)

24. ENS Economic Bureau (30 June 2020). Bharat Biotech's COVID vaccine 1st in India to get approval for human trials. https://indianexpress.com/article/india/bharat-biotechs-COVID-vaccine-1st-in-india-to-get-approval-for-human-trials-6482403/ (last accessed 17 June 2021)

25. Folegatti, P. M., Ewer, K. J., Aley, P. K., Angus, B., Becker, S., & Belij-Rammerstorfer, S. (2020). Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. The Lancet, 467-478.

26. Ghosh, P. (14 May 2021). Centre pins hopes on 5 COVID vaccines apart from Covishield, Covaxin, Sputnik. Hindustan Times.https://www.hindustantimes.com/india-news/centre-pins-hopes-on-5-COVID-vaccines-apart-from-Covishield-Covaxin-sputnik-101620963914257.html (last accessed 24 May 2021).

27. Gill, P. (20 April 2021). 4.6 million doses of COVID-19 vaccine were wasted in India — enough to vaccinate half of Bangalore. Business Insider India. https://www.businessinsider.in/science/health/news/4-6-million-doses-of-COVID-19-vaccine-were-wasted-in-india-enough-to-vaccinate-half-of-bangalore/articleshow/82165181.cms (last accessed 28 May 2021)

28. Holder, J. (13 May 2021). Tracking Coronavirus Vaccinations Around the World. The New York Times. https://www.nytimes.com/interactive/2021/world/COVID-vaccinations-tracker.html (last accessed 13 May 2021)

29. HVA Online (16 May 2021). Vaccine Development, Testing, and Regulation. https://www.historyofvaccines.org/content/articles/vaccine-development-testing-and-regulation (last accessed 16 May 2021).

30. IBEF Report (September 2009). Pharmaceuticals - September 2009. https://www.ibef.org/download/Pharma_171109.pdf (last accessed 9 May 2021)

31. ICMR (March 2021). India's fight against COVID-19 pandemic in crucial stage. E-Samvaad newsletter. https://www.icmr.gov.in/pdf/press_realease_files/Newsletter_English_March_2021.pdf

32. ICMR Website (13 May 2020b). ICMR is partnering in WHO Global Solidarity Trial for Treatment of COVID-19: Being rolled out on fast-track. https://www.icmr.gov.in/pdf/press_realease_files/Press_Release_WHO_Solidarity_Trials.pdf (last accessed 21 May 2021).

33. ICMR Website (9 May 2020a). Indian Council of Medical Research (ICMR) partners with Bharat Biotech International Limited (BBIL) for developing indigenous COVID-19 vaccine. https://main.icmr.nic.in/sites/default/files/press_realease_files/ICMR_Press_Release_09052020.pdf (last accessed 21 May 2021).

34. India Today Web Desk (23 April 2020). This is not a time to make money, says Indian partner of Oxford vaccine attempt. https://www.indiatoday.in/business/story/this-is-not-a-time-to-make-money-says-indian-partner-of-oxford-vaccine-attempt-1669918-2020-04-22 (last accessed 17 June 2021)

35. India Today Web Desk (27 March 2021). Covovax trials begin in India, launch hopefully in September: Adar Poonawalla. India Today. https://www.indiatoday.in/coronavirus-outbreak/vaccine-updates/story/covovax-trials-begin-in-india-serum-institute-novavax-adar-poonawalla-1784381-2021-03-27 (last accessed 24 May 2021).

36. InvestIndia (6 May 2020). https://static.investindia.gov.in/s3fs-public/2020-05/PharmaBrochure_v7_Non%20Paginate.pdf (last accessed 9 May 2021)

37. InvestIndia Website (9 May 2021). Indian pharmaceuticals - a formula for success. https://www.investindia.gov.in/sector/pharmaceuticals (last accessed 9 May 2021)

38. JHU (15 May 2020). COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University. https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6 (last accessed 15 May 2020)

39. Kapoor, A. and Goyal, S. (13 October 2020) How Ministry of Textiles Developed the Indigenous Supply Chain in India for Manufacturing of High-Quality PPEs and Testing Swabs During COVID-19 Pandemic Situation? https://iasmantra.com/wp-content/uploads/2020/11/Ministry-of-Textiles-Report-by-IFC.pdf

40. Kar, S. (16 May 2021). Russia All Set to Launch 'Sputnik Lite' Single-Dose Vaccine in India. India.com. https://www.india.com/news/india/russia-all-set-to-launch-sputnik-lite-single-dose-vaccine-in-india-4668338/ (last accessed 17 May 2021).

41. Kumar, S. (14 May 2021). COVID-19 Vaccination Latest News Today: Covaxin vs Covishield, which is better? - check full details here. Zee Business. https://www.zeebiz.com/india/news-COVID-19-vaccination-latest-news-today-Covaxin-vs-Covishield-which-is-better-check-full-details-here-156679 (last accessed 17 May 2021).

42. Mahalingam, S., & Taylor, A. (20 September 2020). The Pros and Cons of Different COVID Vaccine Technologies Explained. The National Interest. https://nationalinterest.org/blog/reboot/pros-and-cons-different-COVID-vaccine-technologies-explained-169291 (last accessed 13 May 2021)

43. MoHFW FAQs (5 May 2021). https://www.mohfw.gov.in/COVID_vaccination/vaccination/faqs.html#about-the-vaccine (last accessed 5 May 2021)

44. MoHFW Notification (19 April 2020a). A high-level task force, co-chaired by Member, NITI AAYOG and Principal Scientific Adviser, formed to enable COVID-19 related research and vaccine development: Health Ministry. Press Information Bureau. https://pib.gov.in/PressReleseDetail.aspx?PRID=1616154 (last accessed 19 May 2021)

45. MoHFW Notification (19 April 2020b). Updates on COVID-19. Press Information Bureau. https://pib.gov.in/PressReleasePage.aspx?PRID=1616084 (last accessed 19 May 2021)

46. MoHFW Notification (3 August 2020). DCGI approves Phase II+III trials of Oxford University vaccine by Serum Institute, Pune. Press Information Bureau. https://pib.gov.in/PressReleasePage.aspx?PRID=1643136 (last accessed 17 June 2021)

47. MoHFW Notification (18 September 2020). Procedure for Research on Vaccine. Press Information Bureau https://pib.gov.in/PressReleasePage.aspx?PRID=1656188 (last accessed 30 June 2021)

48. MoHFW Notification (30 Dec 2020). Ministry of Health & Family Welfare 2020 ACHIEVEMENTS. Press Information Bureau. https://pib.gov.in/PressReleasePage.aspx?PRID=1684546 (last accessed 17 June 2021)

49. MoHFW Notification (3 March 2021). Phase 3 Clinical Trial of Covaxin, developed by ICMR & Bharat Biotech, shows 81% efficacy. Press Information Bureau. https://pib.gov.in/Pressreleaseshare.aspx?PRID=1702293 (last accessed 19 May 2021)

50. MoHFW Notification (07 March 2021). "Some countries are indulging in vaccine nationalism": Dr Harsh Vardhan. Press Information Bureau. https://pib.gov.in/PressReleasePage.aspx?PRID=1703017 (last accessed 29 Nov 2021)

51. MoHFW Notification (13 April 2021). Centre fast tracks Emergency Approvals for foreign produced

COVID-19 Vaccines that have been granted EUA in other countries to Expand the Basket of Vaccines for Domestic Use and Hasten the Pace and Coverage of Vaccination. Ministry of Health and Family Welfare. https://pib.gov.in/PressReleaseIframePage.aspx?PRID=1711381 (last accessed 17 May 2021).

52. MST (2020). DBT-BIRAC Call on COVID-19 Research Consortium. DBT India. https://dbtindia.gov.in/sites/default/files/uploadfiles/BIRAC.pdf

53. MST Notification (10 May 2020). DBT-BIRAC COVID-19 Research Consortium. Press Information Bureau. https://pib.gov.in/PressReleasePage.aspx?PRID=1622757 (last accessed 21 May 2021)

54. MST Notification (2 July 2020). Government launches Drug Discovery Hackathon 2020 (DDH2020), a first of its kind National Initiative for supporting drug discovery process. Press Information Bureau. https://pib.gov.in/Pressreleaseshare.aspx?PRID=1635928 (last accessed 21 May 2021)

55. MST Notification (August 2020) Dr. Harsh Vardhan announces the successful completion of first Pan India 1000 Genome sequencing of SARS- CoV-2. Press Information Bureau. https://pib.gov.in/PressReleasePage.aspx?PRID=1642869 (last accessed 13 July 2021)

56. MST Notification (29 November 2020). Government Launches Mission COVID Suraksha to accelerate Indian COVID-19 Vaccine Development. Press Information Bureau. https://pib.gov.in/PressReleaseIframePage.aspx?PRID=1676998 (last accessed 21 May 2021).

57. MST Notification (19 January 2021). Year Ender 2020---Department of Biotechnology (DBT)-M/o S & T. Press Information Bureau. https://pib.gov.in/PressReleseDetailm.aspx?PRID=1689929 (last accessed 13 July 2021)

58. MST Notification (7 June 2021). DBT-ILS establishes Animal Challenge Study Platform. DBT India. https://dbtindia.gov.in/pressrelease/dbt-ils-establishes-animal-challenge-study-platform (last accessed 13 July 2021)

59. MST Notification (4 July 2021). Government Readies Two more Central Drug Laboratories at Pune and Hyderabad for COVID Vaccine Testing. DBT India https://dbtindia.gov.in/pressrelease/government-readies-two-more-central-drug-laboratories-pune-and-hyderabad-COVID-vaccine (last accessed 13 July 2021)

60. Nair, G. (10 September 2020). Serum Institute opens world's largest vaccine facility. The Financial Express. https://www.financialexpress.com/industry/capacity-expansion-serum-institute-opens-worlds-largest-vaccine-facility/1701313/ (last accessed 17 June 2021)

61. Novavax (27 May 2020). Novavax Expands Large-Scale Global Manufacturing Capacity. https://ir.novavax.com/news-releases/news-release-details/novavax-expands-large-scale-global-manufacturing-capacity (last accessed 17 June 2021)

62. Novavax (6 August 2020). Novavax and Serum Institute of India Announce Development and Commercial Collaboration. https://ir.novavax.com/news-releases/news-release-details/novavax-and-serum-institute-india-announce-development-and (last accessed 17 June 2021)

63. Pandey, A. (24 April 2021). Biological E gets nod to start Phase III clinical trial of COVID vaccine. India Today. https://www.indiatoday.in/coronavirus-outbreak/vaccine-updates/story/biological-e-phase-iii-clinical-trial-COVID-vaccine-1794623-2021-04-24 (last accessed 24 May 2021).

64. Parashar, S. (14 May 2021). Russia's Sputnik V COVID-19 vaccine to be available in India by next week,

here's all you need to know. Zee News. https://zeenews.india.com/india/russia-s-sputnik-v-COVID-19-vaccine-to-be-available-in-india-by-next-week-here-s-all-you-need-to-know-2361802.html (last accessed 17 May 2021).

65. PIB Press Release (3 January 2021). Press Statement by the Drugs Controller General of India (DCGI) on Restricted Emergency approval of COVID-19 virus vaccine. Press Information Bureau. https://www.icmr.gov.in/pdf/press_realease_files/HFW_DCGI_energency_use_authorisation_03012021_2.pdf (last accessed 29 Nov 2021)

66. Pilla, V. (7 December 2020). This is how DBT is helping companies accelerate development of COVID-19 vaccine. Moneycontrol. https://www.moneycontrol.com/news/business/companies/this-is-how-dbt-is-helping-companies-accelerate-development-of-COVID-19-vaccine-6200741.html (last accessed 13 July 2021)

67. Prasad, R. (23 April 2020). Coronavirus: Phase-1 human trial of Oxford University vaccine to begin today. The Hindu. https://www.thehindu.com/sci-tech/science/coronavirus-phase-1-human-trial-of-oxford-university-vaccine-to-begin-today/article31412055.ece (last accessed 21 May 2021).

68. Prasad, R. (22 July 2020). Coronavirus | Serum Institute has begun manufacturing Oxford COVID-19 vaccine. The Hindu. https://www.thehindu.com/sci-tech/science/serum-institute-has-begun-manufacturing-oxford-coronavirus-vaccine/article32158160.ece (last accessed 17 June 2021).

69. PTI (4 Jan 2021). Zydus Cadila gets DCGI nod to initiate Phase-3 clinical trials for COVID-19 vaccine. Money Control. https://www.moneycontrol.com/news/trends/health-trends/zydus-cadila-gets-dcgi-nod-to-initiate-phase-3-clinical-trials-for-COVID-19-vaccine-6298521.html (last accessed 24 May 2021).

70. PTI (6 December 2020). Clinical trial: 17 volunteers given Russia's Sputnik V COVID-19 vaccine in Pune. The Indian Express. https://indianexpress.com/article/india/clinical-trial-17-volunteers-given-russias-sputnik-v-COVID-19-vaccine-in-pune-7094153/ (last accessed 24 May 2021).

71. Raghavan, P. (28 July 2020). Amidst race for vaccine, govt readies trial sites, detailed data on volunteers. The Indian Express. https://indianexpress.com/article/india/amidst-race-for-COVID-vaccine-govt-readies-trial-sites-detailed-data-on-volunteers-6526694/ (last accessed 13 July 2021)

72. Raghavan, P. (15 December 2020). Pune-based Gennova to begin human trials of its COVID vaccine 'soon'. The Indian Express. https://indianexpress.com/article/india/pune-based-gennova-to-begin-human-trials-of-its-COVID-vaccine-soon-7105081/ (last accessed 24 May 2021).

73. Raghavan, P. (30 April 2021). Explained: Why does India need COVID-19 vaccine ingredients from US? Indian Express. https://indianexpress.com/article/explained/us-embargo-raw-materials-Covishield-covovax-production-COVID-19-vaccine-7280711/ (last accessed 16 May 2021)

74. Ramesh, S and Yadavar, S. (25 April 2020). Why South Asia has 20% of world's population but less than 2% of COVID-19 cases. The Print. https://theprint.in/health/why-south-asia-has-20-of-worlds-population-but-less-than-2-of-COVID-19-cases/408471/ (last accessed 17 June 2021)

75. Reddy, G. (2020, April 17). Swarajyamag.com. Leadership Lessons From India During The Covid-19 Crisis. Swarajaya. Retrieved from- Leadership Lessons From India During The Covid-19 Crisis.

76. Sarkar, S (9 June 2021). Covaxin effective in neutralising Delta, Beta variants of Covid-19: Study. Hindustan Times.

77. Saxena, A. (25 July 2020). Delhi: 30-year-old is first to get dose of trial drug Covaxin. The Indian Express. https://indianexpress.com/article/india/aiims-administers-first-dose-of-bharat-biotechs-potential-COVID-vaccine-to-30-yr-old-man-6521778/ (last accessed 19 May 2021)

78. Sen, M. (2 January 2021). India's 1st COVID-19 vaccines: DCGI approves Serum, Bharat Biotech vaccines for emergency use. Livemint. https://www.livemint.com/news/india/indias-first-vaccines-dcgi-approves-bharat-biotech-s-Covaxin-and-sii-s-Covishield-11609650896132.html (last accessed 19 May 2021)

79. Sethu, D. (17 February 2021). India's Journey From Requesting Penicillin in 1947 to Making Vaccines for the World. The Better India. https://www.thebetterindia.com/249438/india-COVID-19-vaccine-hub-Covishield-serum-institute-narendra-modi-justin-trudeau-canada-partition-penicillin-malaria-history-div200/ (last accessed 12 May 2021).

80. Siddiqui, Z. (28 April 2020). India's Serum Institute to make millions of potential coronavirus vaccine doses. The Reuters. https://www.reuters.com/article/us-health-coronavirus-india-vaccine-idUSKCN22A2YY (last accessed 17 June 2021).

81. Sirur, S. (21 April 2021). US embargo on exporting COVID vaccine raw materials and how it could impact India. The Print. https://theprint.in/theprint-essential/us-embargo-on-exporting-COVID-vaccine-raw-materials-and-how-it-could-impact-india/643374/ (last accessed 16 May 2021)

82. The Hindu (23 October 2020). Coronavirus | Covaxin Phase III trial from November. https://www.thehindu.com/business/Covaxin-phase-iii-trial-from-november/article32928549.ece (last accessed 19 May 2021).

83. The Live Mirror (12 October 2021). COVID-19: Covaxin Vaccine Approved For Children Between 2 to 18 (last accessed 12 October 2021)

84. U.S. Department of Health and Human Services (2021). https://www.hhs.gov/immunization/basics/types/index.html (last accessed 17 June 2021).

85. WHO (29 June 2020). Listings of WHO's response to COVID-19. https://www.who.int/news/item/29-06-2020-COVIDtimeline (last accessed 17 June 2021).

86. WHO (8 December 2020). How are vaccines developed? World Health Organization. https://www.who.int/news-room/feature-stories/detail/how-are-vaccines-developed?gclid=CjwKCAjwhYOFBhBkEiwASF3KGVpZpy5OPl2XcFdutm_1D5QMFvdJa1NPfuweGY2RLAEDD4obkLY0bBoCfNsQAvD_BwE (last accessed 16 May 2021).

87. WHO (12 January 2021) The different types of COVID-19 vaccines. https://www.who.int/news-room/feature-stories/detail/the-race-for-a-COVID-19-vaccine-explained (last accessed 17 June 2021).

Note: All images used in the report are for representation purposes only

IFC | INSTITUTE *for* COMPETITIVENESS

Institute for Competitiveness, India (IFC) is the Indian knot in the global network of the Institute for Strategy and Competitiveness at Harvard Business School. IFC India is an international initiative dedicated to the enlarging and purposeful dissemination of the body of research and knowledge on competition and strategy, as pioneered over the last 25 years by Professor Michael Porter of the Institute for Strategy and Competitiveness at Harvard Business School. Institute for Competitiveness, India conducts and supports indigenous research, offers academic and executive courses, provides advisory services to the corporate and government sectors, and organises events. The institute studies competition and its implications for company strategy; the competitiveness of nations, regions, and cities and thus, generates guidelines for businesses and those in governance and suggests and provides solutions to socio-economic problems.

www.competitiveness.in

• • •

The Institute for Competitiveness

U24/8, U-24 Road, U Block, DLF Phase 3, Sector 24, Gurugram, Haryana 122022 info@competitiveness.in | www.competitiveness.in