

Perspective

India`s role in COVID-19 vaccine diplomacy

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Teaser / Highlights

Indian vaccine manufacturers such as Serum Institute of India, Bharat Biotech, Dr. Reddy's Laboratories, Biological E Limited, Aurobindo Pharma, and Indian Immunologicals have already secured the license to manufacture major vaccine candidates. The ability of the country to manufacture cost-effective COVID-19 vaccines will help to meet the global vaccine requirements.

Key words: COVID-19; SARS-CoV-2; Vaccine diplomacy; India; Vaccination coverage; Vaccine

India is regarded as the vaccine manufacturing hub of the world, contributing 60% to the global vaccine supply.¹ The country has the capacity to manufacture well over 3 billion coronavirus disease 2019 (COVID-19) vaccine doses annually.² The ability of the country to produce low-cost COVID-19 vaccines will benefit low-income countries that cannot afford expensive vaccines.³ Majority of the Indian vaccine manufacturers have signed exclusive license agreements with foreign collaborators for developing and manufacturing COVID-19 vaccines.² Covaxin (BBV152) is India's first indigenous COVID-19 inactivated vaccine developed and manufactured by Bharat Biotech in collaboration with the Indian Council of Medical Research (ICMR) and the National Institute of Virology (NIV). The recent findings indicate that Covaxin can effectively neutralize the recently emerged B.1.1.7 SARS-CoV-2 variant (UK variant).⁴ Bharat Biotech has also initiated the phase 1 trial (NCT04751682) of single-dose adenovirus vectored intranasal vaccine (BBV154) for COVID-19. Covishield is the Indian version of the replication-deficient adenoviral vector vaccine developed by Oxford University and AstraZeneca (AZD1222, previously called ChAdOx1 nCoV-19 vaccine). It is manufactured by the Serum Institute of India (SII), the world's largest vaccine manufacturer and one of the leading exporters of vaccines. SII has also collaborated with Codagenix to manufacture COVI-VAC, a live-attenuated intranasal vaccine against COVID-19.³ According to the Department of Biotechnology (DBT), India has the capacity to manufacture 70-100 million doses of Covishield vaccine per month. In comparison, the indigenously developed Covaxin is limited to 150 million doses per year.⁵

The major Indian vaccine manufacturers such as SII (Covishield, Covovax, and COVI-VAC), Bharat Biotech (BBV154), Dr. Reddy's Laboratories (Sputnik V), Biological E Limited (Janssen Ad26.COVID-19), Aurobindo Pharma (UB-612), and Indian Immunologicals (Live attenuated SARS-CoV-2 vaccine developed by Griffith University), have also secured the license to manufacture vaccine candidates developed in

other countries (Table 1).^{2,6} In addition to that, indigenously developed vaccine candidates such as ZyCoV-D (plasmid-based DNA vaccine), HGCO19 (mRNA vaccine), and Mynvax COVID-19 vaccine (RBD-based subunit vaccine) are also making significant progress in pre-clinical/clinical studies.⁶ Among the vaccine candidates, ZyCoV-D (Zydus Cadila), Sputnik V (Dr. Reddy's Laboratories), Covovax (Serum Institute of India, SII), Bio E COVID-19 (Biological E Limited), BBV154 (Bharat Biotech), and HGCO19 (Gennova Biopharmaceuticals) are undergoing human clinical trials in India.⁶ ZyCoV-D is an indigenous DNA vaccine candidate developed by Zydus Cadila with the support of the Biotechnology Industry Research Assistance Council (BIRAC).³ The vaccine received approval from the Drugs Controller General of India (DCGI) to conduct phase III clinical trials. COVID-19 vaccine development in India is led by DBT with the help of BIRAC under the scheme "Mission COVID Suraksha," an initiative to accelerate the development (pre-clinical/clinical development) of major vaccine candidates. The initiative also aims to enable the development of indigenous, cost-effective, and accessible vaccines.⁷ Mynvax, an Indian Institute of Science incubated startup, has developed a highly thermotolerant, immunogenic COVID-19 vaccine candidate that does not require refrigeration and can be stored at 37°C for four weeks. The efficacy of the vaccine candidate is already established in guinea pigs.⁸ The thermotolerant vaccine candidate developed by Mynvax will be a game-changer if it clears the clinical trials. Such a vaccine will be the ideal candidate for deployment in remote areas that lack cold chain facilities.

Following the successful roll-out of COVID-19 vaccines across the globe, several countries have initiated large-scale vaccination programs as an effort to control the ongoing pandemic (<https://ourworldindata.org/covid-vaccinations>). India has initiated a country-wide vaccination program in early 2021 and has vaccinated 87.1 million people as of April 8, 2021 (<https://www.mygov.in/covid-19>). At present, Covaxin and Covishield vaccines are being used for the vaccination drive in India as they are the only vaccines that have received approval (restricted use in emergency situation) from the Central Drugs and Standards Committee (CDSCO).⁶ The country has recently initiated "Vaccine Maitri" (*Maitri* means friendship in Hindi), a diplomatic mission to supply vaccines (Covaxin and Covishield) to the needy countries.¹ Under this initiative, India has already supplied vaccines to countries such as Bangladesh (3.3 million doses), Myanmar (1.7 million), Nepal (1.1 million), Sri Lanka (0.5 million), Afghanistan (0.5 million), Maldives (0.2 million), Guatemala (0.2 million), Nicaragua (0.2 million), Bhutan (0.55 million), Mongolia (0.15 million), Mauritius (0.1

million), Bahrain (0.1 million), Oman (0.1 million), Kenya (0.1 million), Uganda (0.1 million), Paraguay (0.1 million), Fiji (0.1 million), and Mozambique (0.1 million).⁹ The Caribbean Community countries, including Barbados, Dominica, Saint Lucia, Saint Kitts and Nevis, Saint Vincent and the Grenadines, Suriname, Antigua and Barbuda, Jamaica, Guyana, Belize, and the Bahamas have also received vaccines as a grant from India.⁹ India has also donated 0.2 million doses of the Covishield vaccine for vaccinating the United Nations peacekeepers. This is in addition to the 18.1 million vaccine doses (Covishield) that India has already supplied to different countries under the COVID-19 Vaccines Global Access (COVAX), a global initiative coordinated by the World Health Organization (WHO), the Coalition for Epidemic Preparedness Innovations, and Gavi, the Vaccine Alliance (<https://www.gavi.org/vaccineswork/covax-explained>).⁹ India's commitment to supporting equitable access to vaccines is evident from the efforts made by the country to supply vaccines as either grants or commercial supplies. India has also called on the World Trade Organization to temporarily suspend the intellectual property rights of COVID-19 vaccines, which will ensure fair and equitable access to vaccines.^{1,10} Although the proposal was supported by the WHO Director-General, it encountered severe opposition from the United States, the United Kingdom, Canada, Norway, and the European Union.¹⁰

India has also dispatched 35.79 million doses of the COVID-19 vaccine to various countries as commercial exports.⁹ However, India has recently limited the expansion of COVID-19 vaccine exports to fuel the country-wide vaccination drive. The announcement came in following the initiation of the second wave and the rapid increase of COVID-19 cases in several parts of the country. Being a leader in vaccine manufacturing, India's ability to offer complimentary COVID-19 vaccines to low-income countries, especially the immediate neighbors, will not only help strengthen its ties with partner countries but also achieve equitable access to vaccines. Furthermore, India's move to provide vaccine assistance to low and middle-income countries will boost the efforts in achieving global vaccination coverage. India's ability to develop and manufacture cost-effective COVID-19 vaccines on a large scale will help to meet the global vaccine requirements without causing an additional economic burden.

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Declaration of Interest

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Author contributions

KS and KD conceptualized the manuscript; KS wrote the first draft with input from KD; all authors contributed to revisions and approved the final manuscript.

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Vaccine	Efficacy	Vaccine Platform	Developer	Manufacturer in India	Status
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Table 1: The major vaccines and vaccine candidates developed and/or manufactured in India.

Covaxin (BBV152)	80.6% (Interim analysis)	Whole- virion inactivated Vero cell derived platform	Bharat Biotech in collaboration with the Indian Council of Medical Research and the National Institute of Virology	Bharat Biotech	Emergency Use Authorization (EUA) granted in India. Capacity to manufacture 150 million doses per year. Supplied to Sri Lanka, Mongolia, Myanmar, Bahrain, Oman, Philippines, Maldives and Mauritius via government-to- government deals. Ocugen and Bharat Biotech signed deal to co- develop and manufacture Covaxin for the United States market.
Covishield (AZD1222)	70.4%	Replication- deficient adenoviral vectored vaccine	Oxford University and AstraZeneca	Serum Institute of India (SII)	EUA granted in India. Capacity to manufacture 70-100 million doses per month. SII is offering the vaccine at a cost of less than \$3 per dose making it the cheapest COVID-19 vaccine in the world.

Sputnik V (Gam-COVID-Vac)	91.6%	Recombinant adenovirus vaccine (rAd26 and rAd5)	Gamaleya National Research Institute of Epidemiology and Microbiology	Dr. Reddy's Laboratories, Virchow Biotech, Stelis Biopharma, Gland Pharma, Hetero Biopharma, and Panacea Biotech	Russian Direct Investment Fund (RDIF) signed production contracts with Virchow Biotech (200 million doses per year), Stelis Biopharma (200 million), Gland Pharma (252 million), Hetero Biopharma (100 million), and Panacea Biotech (100 million). Dr. Reddy's Laboratories signed production and distribution contract with RDIF to supply Sputnik V vaccine in India (250 million doses per year).
Janssen Ad26.COVS.2.S (JNJ-78436735)	66.1%	Replication-incompetent adenovirus (Ad26) vectored vaccine	Johnson & Johnson (Janssen Pharmaceuticals)	Biological E Limited	Technology transfer between Johnson & Johnson and Biological E Limited to expand the manufacturing capabilities. A deal was made to manufacture 1 billion vaccine doses by the end of 2022.
Covovax (NVX-CoV2373)	89.3%	Recombinant spike protein nanoparticle vaccine	Novavax with funding from Coalition for Epidemic Preparedness	Serum Institute of India	SII has already received the licence to manufacture and supply the

			Innovations (CEPI)		vaccine in low- and middle-income countries as well as India. In addition to that, Novavax and SII have committed to deliver 1.1 billion doses to the COVID-19 Vaccine Global Access (COVAX) facility.
ZyCoV-D	-	DNA vaccine (plasmid vector)	Zydus Cadila, India	Zydus Cadila	Approved by Drugs Controller General of India (DCGI) to conduct Phase III clinical trial (30,000 volunteers) in India. Zydus Cadila plans to expand ZyCoV-D production capacity to 150 million doses a year.
BBV154	-	Replication-deficient adenoviral vectored intranasal vaccine	Washington University School of Medicine in collaboration with Bharat Biotech and Precision Virologics	Bharat Biotech	Initiated the Phase 1 trial (safety and Immunogenicity) of single-dose adenovirus vectored intranasal vaccine (NCT04751682). Precision Virologics has optioned rights for Europe, USA, and Japan while Bharat Biotech has

					retained rights for all other markets.
Bio E COVID-19 (BECOV2A, BECOV2B, BECOV2C and BECOV2D)	-	SARS-CoV-2 RBD protein-based subunit vaccine	Baylor College of Medicine, Biological E Limited, and Dynavax Technologies Corporation	Biological E Limited	The vaccine candidate has received funding from the Department of Biotechnology, India. Coalition for Epidemic Preparedness Innovations (CEPI) will contribute \$5 million to scale up the vaccine production. This will potentially enable Biological E Limited to produce 100 million doses in 2021. If proven to be safe, immunogenic, and effective, the vaccine will be made available for procurement and allocation via COVAX facility
HGCO19	-	mRNA vaccine	Genova Biopharmaceuticals in collaboration with HDT Biotech Corporation	Genova Biopharmaceuticals	HGCO19 is the first indigenous mRNA vaccine candidate. Safety and immunogenicity study conducted in rodent and non-human primate models. Unlike Pfizer-

					BioNTech mRNA vaccine (BNT162b2), HGC019 can be stored at 2 to 8°C.
COVI-VAC	-	Intranasal, live-attenuated vaccine	Codagenix, United States	Serum Institute of India	Undergoing Phase 1 trial (safety and immunogenicity) (NCT04619628). SII has initiated the production of COVI-VAC in India for Phase 1 clinical trial.
UB-612	-	Multitope peptide-based vaccine	Covaxx, United States	Aurobindo Pharma	Aurobindo Pharma has signed exclusive license agreement with Covaxx to develop, manufacture, and commercialise UB-612 vaccine for India and United Nations International Children's Emergency Fund (UNICEF). Aurobindo Pharma has a production capacity of 400-450 million COVID-19 vaccine doses.
Live attenuated SARS-CoV-2 vaccine	-	Live-attenuated vaccine	Griffith University, Australia	Indian Immunologicals	Indian Immunologicals has signed research collaboration agreement with Griffith

					University to develop the vaccine. They are planning to use Vero cell platform technology for mass production of the vaccine.
Mynvax COVID-19 vaccine	-	Mammalian cell-expressed, glycan-engineered, RBD-based subunit vaccine	Mynvax and Indian Institute of Science	No production facility	Highly thermotolerant lyophilized vaccine can be stored for at least 4 weeks without refrigeration (37°C). The vaccine can also withstand 70° C for around 16 hours. Promising results in several animal models (mice, guinea pigs, and hamsters). Mynvax lacks a vaccine production facility. The company is in talks with other manufacturers for production and further trials in humans.