



## India & its Indigenous Covid-19 Vaccines

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### Abstract

The global economy is recovering much faster than expected. The key for this lock called Covid-19 is vaccinations. Clearly, for fighting against pandemics, the vaccine is the most crucial & potent bullet to shoot on the potential virus, in this case, it's SARS-CoV-2.

India is a dynamic cum diverse country with a huge population distributed unevenly around the country. But whatever the distribution of the country is, equality and transparency in vaccine availability are quintessential. The Covid-19 pandemic has hit India hard in all domains, so a successful vaccination drive or the World's largest vaccination drive was needed to be delivered to all the citizens without delay, and it started on January 2021. India's vaccines are still playing a major role in vaccine export to lower- & middle-income countries with COVAX along with external exports via the production companies. The equity of vaccines around the globe should always be the utmost priority.

Here in this article, the potential vaccine candidatures in use in India will be discussed. India's Biotech cum pharma companies indigenously came up with several novel vaccines, a couple of which are not yet completely done with WHO regulatory approvals but are in process. But all these vaccines have received Emergency use authorization (EUA) from the Drug Controller General of India (DCGI) and a couple has received regular marketing authorization as well. What makes it more interesting is that these vaccines include the World's first DNA vaccine ever approved for use in humans

**Keywords:** India, Vaccine, DCGI, EUA, Covid-19, Pandemic, COVAX

### Introduction

India being the second-most populous country in the world, the demand for vaccines was assumed to be always high and equal distribution and availability for all was another big hurdle. India has so far approved 9 vaccines for EUA, out of which 2 have already received regular use authorization. All the vaccines in India are available at a considerable price in private institutions and available for free in government institutions. The booster doses dubbed as precautionary doses in India started from 10th January 2022, people are allowed to give booster

doses of the same vaccine which they took as 1st & 2nd dose, i.e., Covishield or Covaxin which are locally produced. Corbevax & ZyCoV-D or any other vaccines haven't made the cut yet for booster doses in India.

It is imminent from the Table below that a number of Indian Biotech companies came ahead for the production and immunization of the whole Indian population plus for helping out COVID-19 Vaccines Global Access (COVAX), GAVI & CEPI to

distribute vaccines to countries in need along with private exports to the Indian subcontinents, Asia's middle-east, Caribbean nations, African countries to name a few. Out of all the Biotech companies mentioned above, the Serum Institute of India is the World's largest vaccine producer. India has always tried to develop vaccines in a way that is cost-effective and also India has a good history of exporting vaccines at no or affordable price ranges like the Polio or Rotavirus vaccine. This ongoing Covid -19 pandemic is no different, in this case as well India is successfully exporting vaccines [1] [2] [3].

### Main Text

The Covid-19 pandemic observed a plethora of vaccines and even the exploration of new types of formulation came forward, which were thought off and were in trials but were not approved for commercial use like the DNA vaccine by Zydus Cadila/mRNA vaccines by Moderna & Pfizer. Before this pandemic, it was always believed that vaccines take around 8 to 12 years with clinical trials included, before it is fully approved for commercial human use. Though in cases like pandemics approvals by

regulatory bodies come thick and fast for rolling out vaccination campaigns as quickly as possible. It is imminent from India's vaccine policy that India tried to establish a Make in India vaccine policy and was reluctant to offer indemnity bond to any of the vaccines whether made by Indian Biotech firms or abroad Biotech firms. Approving vaccines don't come easy in a country like India as the special Covid Taskforce and the DCGI need to consider various factors regarding the stability, transportation & storage of the vaccines as the vaccine vials need to reach the people regardless of where they stay within the country [4]. So, an achievable storage temperature plays a major role, too low of a storage temperature may not be feasible in every domain of the country & also then transportation becomes difficult, especially to rural areas where there are limited or no vehicles which can provide such low temperatures or such storing facilities.

It should be noted that, though mixing two different types of vaccines showed interesting results but it's not yet approved in India due to lack of trials in this case.

**Table 1: Various vaccines are in production in India. In this table the vaccines approved for Emergency Use Authorization (EUA) in India has been mentioned.**

Vaccine	Developer	Type	Manufacturing Location	Special Information
<b>Covishield</b> (Approved for regular use authorization)	Serum Institute of India (Oxford/AstraZeneca formulation)	Non-replicating adenoviral vector vaccine	India	Covishield made by Serum Institute of India (SII) is the Indian made version of Vaxzevria (UK). (Oxford/AstraZeneca formulation)
<b>Covaxin</b> (Approved for regular use authorization)	Bharat Biotech	Whole-Virion Inactivated Vero cell line	India	India's first indigenous vaccine to be approved in India as well as by WHO.

<b>Covovax</b>	Serum Institute of India (Novavax formulation)	Recombinant spike protein nanoparticle vaccine	India	Covovax is mass produced in India by SII. (Novavax formulation)
<b>Corbevax</b>	Biological E	Recombinant protein sub-unit vaccine	India	Corbevax developed by Indian pharma company Biological E in collaboration with US-based Dynavax and Baylor College of Medicine.
<b>Janssen</b>	Johnson & Johnson	Adenoviral vector vaccine (Single dose vaccine)	USA	Janssen is world's first approved single dose Covid-19 vaccine.
<b>Spikevax</b>	Moderna	mRNA vaccine	USA	The Covid-19 pandemic brought the breakthrough mRNA vaccines needed.
<b>Sputnik V</b>	Serum Institute of India, Gland Pharma, Hetero Biopharma, Panacea Biotec, Stelis Biopharma, Virchow Biotech and Morepen Laboratories, Dr. Reddy's Laboratories (Gamaleya formulation - Russia)	Recombinant Adenovirus vaccine	India	Sputnik V is being mass produced in India via several Biotech companies in India with Dr. Reddy's Laboratories pivoting all the action.  (Gamaleya formulation - Russia)

<b>Sputnik Light</b>	Serum Institute of India, Gland Pharma, Hetero Biopharma, Panacea Biotec, Stelis Biopharma, Virchow Biotech and Morepen Laboratories, Dr. Reddy's Laboratories (Gamaleya formulation - Russia)	Adenoviral vector vaccine (Single dose vaccine)	India	Sputnik Light is being mass produced in India via several Biotech companies in India.  (Gamaleya formulation - Russia)
<b>ZyCoV-D</b>	Zyodus Cadila	DNA vaccine	India	The breakthrough of DNA plasmid vaccine, approved for human use for the first time in history.

**Table 1.** List of Vaccines given EUA/Regular use authorization in India for various age groups [13] [10] [14].

### Formulations

A detailed analysis is provided here about the indigenously developed vaccines of India – Covaxin, Corbevax, Zycov-D and the vaccine jab used for inoculating the majority of the population of India - Covishield. India is still in the midst of approving vaccines for various age groups, expert regulatory bodies are regularly going through trial results and other composition details before giving the nod for a particular vaccine for a certain age group [5].

### Covishield

It is the first vaccine to be approved in India and is rolled out in maximum amount in India (to around 90% of the population) compared to other vaccines. Covishield known as ChAdOx1 nCoV-19 or AZD1222 (Research name) was formulated by the University of Oxford and AstraZeneca. A modified version of a chimpanzee adenovirus (ChAdOx1) is used which can enter human cells but doesn't replicate inside. It is administered through the Intramuscular region. A gene for the coronavirus vaccine was incorporated into the adenovirus DNA, allowing the vaccine to pivot its action towards the

spike proteins that SARS-CoV-2 uses to enter human cells. Covishield is a two-dose vaccine that aims to protect against COVID-19 [6] [7]. It has been developed jointly in the UK, and further mass-produced in the Serum Institute of India (SII) for inoculating Indians and also mass-produced in South Korea. The SII is the largest producer of vaccines around the globe, it is exporting Covishield to the Indian subcontinent, other countries, and also to global vaccine bodies like GAVI. This vaccine is branded by two names Vaxzevria, Covishield. The name Vaxzevria is branded in the UK which is made by AstraZeneca-Oxford University and the name Covishield is branded when it is produced by the Serum Institute in India.

SII has the capacity of producing around 2.4 million doses in a single day and around 100 million doses a month. The gap between the respective two doses of Covishield/Vaxzevria can be varied from 4 weeks to 12 weeks, the tenure is generally decided by the public health departments of the countries using this vaccine. The tenure is greatly influenced by the population, infrastructure and there are even reports

that the greater the tenure (till 12 weeks) better is the efficiency of this vaccine.

Steps in Covishield Manufacture in SII:

1. **Inactivation process** - This involves the antigen preparation step.
2. **Sterilization of components** - The isolated antigen is purified along with other required components.
3. **Formulation** - The purified antigen is combined with adjuvants, stabilizers, and preservatives to form the final vaccine preparation.
4. **Fill-Finish** - Process of filling vials with a vaccine after vials have been fully sterilized (Vials are heated at 305 degrees Celsius and then brought down to 24 degrees Celsius).
5. **Loading, Collection** – These are the only 2 steps done manually.
6. **Vial acceptance process** – A specialized machine is present which at the end accepts/rejects the vial depending on contamination.

### Efficacy

Covishield efficacy against symptomatic Covid-19 after 14 days from taking the 2nd dose is (66-76) % in India. There are different efficacy rates of Covishield/Vaxzevria for different countries due to genetic variations among the populations. Covishield has been deemed to increase antibody levels against Omicron in its third dose after the initial two doses of the same vaccine or mRNA or inactivated vaccines.

### Covaxin

Covaxin (BBV152) has been created indigenously in India by Bharat Biotech in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV). The vaccine has been developed via the traditional Whole-Virion Inactivated Vero cell line platform given through the intramuscular region. The concept of this formulation is simple and has been in the fray for decades now and is, therefore, a tried & tested approach. Inactivated vaccines possess the dead virus and successfully mount a defensive immune response in the host body. It is a 2-dose vaccine with the gap between the two shots variable, decided accordingly by epidemiological regulatory bodies. Covaxin is also manufacturing booster shots and a nasal vaccine

against Covid. Covaxin is approved in India for 18+ adults, as well as recently approved for the age group (15-17) years.

### Efficacy

Covaxin through trials demonstrated a 77.8% vaccine efficiency against volunteers who were symptomatic for SARS-CoV-2.

Efficiency for volunteers showing severe symptoms was 93.4% and 63.6% against asymptomatic individuals for Covid-19 [8].

Covaxin booster has been deemed to be 90% effective against Omicron.

### Corbevax

Corbevax (BECOV2D, BioE COVID-19) is developed by Indian pharma company Biological E in collaboration with US-based Dynavax and Baylor College of Medicine. Corbevax is India's first indigenously developed recombinant protein subunit vaccine. This vaccine is a double dose and is given from the intra-muscular region with a gap of 28 days in between. This receptor binding domain (RBD) protein sub-unit Covid-19 vaccine works on the classic principle of a viral protein antigen, i.e., the spike proteins of SARS-CoV-2, the adjuvants used for enhancing the efficacy of this vaccine are Alum in combination with CpG 1018 [9].

Corbevax has already been approved for EUA on adults in India but is yet to be incorporated in the country's vaccination drive but has been recently approved by the Subject Expert Committee (SEC) and Central Drugs Standard Control Organization (CDSCO) and now has also got the approval of the DCGI for the age group of (12-18) years after Covaxin [10].

### Efficacy

According to Biological E and India's chairperson for Covid Working Group Corbevax has an efficacy of 90% and has been deemed as a game-changer in the fight against the pandemic.

### ZyCoV-D

ZyCoV-D has been formulated by Zydus Cadila and Biotechnology Industry Research Assistance Council (BIRAC). There is a number of DNA vaccines in clinical trials around the globe like in the US, Japan, South Korea, Italy, Canada to name a few but

**ZyCoV-D is the first DNA vaccine to be approved for EUA anywhere in the world. DNA vaccines are based on bacterial plasmids** [11]. Researchers have welcomed this news and has deemed the fact that ZyCoV-D is the first of many DNA vaccines to be used in humans. ZyCoV-D is an achievement in itself for India & its pharma cum Biotech firms [12].

ZyCoV-D is a 3-dose vaccine unlike other vaccines and is administered on day 0, day 28, day 56. Most interestingly it's a needle-free vaccine, it is administered under the skin intradermally. The region under the skin possesses a plethora of immune cells, hence any unidentifiable foreign object is galloped away by these immune cells. The intramuscular region is not favoured in the case of DNA vaccines because the DNA vaccines need to make it to the cell nucleus. Hence a simple reason why DNA vaccines haven't been able to induce a potent immune response and have remained majorly in animal trials since the 1990s.

ZyCoV-D has been approved for children of 12 to 17 years and for use on adults only in 7 Indian states as of now namely Bihar, Maharashtra, West Bengal, Uttar Pradesh, Jharkhand, Tamil Nadu, and Punjab. According to government statements, the vaccine is being used only in those districts where the first dose coverage has been low.

### **Efficacy**

Cadila Healthcare announced their vaccine showed the efficacy of 66.6% against asymptomatic individuals and around 100% against symptomatic moderate or severe individuals.

### **Conclusion**

SARS-CoV-2 has hit the world economy hard and no single country has escaped from its wrath. The variants came thick and fast and overwhelmed the public health backbone in the last two years bringing with it 3 to 4 waves till now. In the midst of all these in a country like India where around half of the population earns on a daily work basis, lockdowns, restrictions, and containment zones were equivalent to no wage, hence no food to them. Lockdowns, restrictions were to save people from the fatal virus but on the other hand, the Indian democratic government had the added burden of people who are daily wage earners. So hence a quick vaccine roll-out seemed the most feasible option. But inoculating the

eligible population of the 1.38 billion with double dose and a potential booster dose was never going to come easy considering all the hurdles from vaccine manufacture to its proper transportation & storage. The Indian pharma cum Biotech industry sector is doing a much more than expected job for bringing in novel vaccines to collaborating with world leaders to produce vaccine jabs at a quick rate for the whole of the eligible population and also to be mentioned the export of vaccines to COVAX and countries in need to maintain the vaccine equity.

The second Covid wave of the Delta variant (Variant of Concern) in India infected millions of people. For this reason, the Indian government temporarily barred the vaccine producers to export vaccines abroad. This was a huge setback for many countries and even for COVAX & GAVI [2]. But when the infection slope started to deteriorate the exports started again.

The majority of the adult Indian population is inoculated now and the focus is now on boosters and inoculating the younger generation (12 to 17) years which is going on largely in schools so that every child in rural or urban area has the access to the jabs.

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All the pharma cum Biotech industries in the world are doing a marvellous job. The government of all the countries along with the global regulatory bodies are also doing a great job to distribute safe, effective vaccines to everyone by maintaining vaccine equity.

### **Author Contributions**

Tathagata Das: Was involved in everything related to this manuscript.

### **Conflict of Interest**

There is no conflict of interest related to this manuscript.

### **Bibliography**

1. C. Chakrabortya and G. Agoramoor, "India's cost-effective COVID-19 vaccine development initiatives," Elsevier, p. 7883–7884, 2020.

2. T. V. Padma, "India's COVID-vaccine woes — by the numbers," 2021.
3. "NITI Aayog," [Online]. Available: <https://www.niti.gov.in/one-billion-doses-indias-leadership-world>.
4. "Ministry of Health & Family Welfare, Government of India," [Online]. Available: <https://www.mohfw.gov.in/>.
5. "Indian Council of Medical Research (ICMR)," [Online]. Available: <https://vaccine.icmr.org.in/covid-19-vaccine>.
6. "Central Drugs Standard Control Organization," [Online]. Available: <https://cdsco.gov.in/opencms/opencms/en/Home/>.
7. E. Dolgin, "The tangled history of mRNA vaccines," 2021.
8. C. o. M. Research, "India COVID-19 Vaccine Tracker," [Online]. Available: <https://analytics.icmr.org.in/public/dashboard/149a9c89-de6d-4779-9326-5e8fed3323b6>.
9. D. G. P. R. S. S. K. R. A. Stuti Pramod, "Effectiveness of Covishield vaccine in preventing Covid-19 – A test-negative case-control study," Elsevier, 2022.
10. R. Kumar, "A Cross Sectional Survey to Assess the Side Effects Associated with Covid-19 Vaccination," International Journal of Medical Science and Current Research, vol. 4, no. 5, pp. 438-442.
11. "COVAXIN® - India's First Indigenous COVID-19 Vaccine," Bharat Biotech, [Online]. Available: <https://www.bharatbiotech.com/covaxin.html#:~:text=The%20indigenous%2C%20inactivated%20vaccine%20is,Ver0%20Cell%20derived%20platform%20technology..>
12. Staff, R. Carlson and H. Lutmer, "CorbeVax COVID-19 Vaccine," Precision Medicine, 2022.
13. Dey, H. Chandra, T. C. Rajanathan, H. P. Pericherla, S. Kumar, H. S. Choonia, M. Bajpai, A. . K. Singh, A. Sinha, G. Saini, P. Dalal, S. Vandriwala, M. . A. Raheem, R. D. Divate, N. L. Navlani, V. Sharma, A. Parikh, S. Prasath, M. S. Rao and . K. Maithal, "Immunogenic potential of DNA vaccine candidate, ZyCoV-D against SARS-CoV-2 in animal models," Elsevier, vol. 39, no. 30, pp. 4108-4116, 2021.
14. S. Mallapaty, "India's DNA COVID vaccine is a world first – more are coming," pp. 161-162, 2021.