WORLD'S FIRST COVID-19 DNA VACCINE: The Scientific Journey
World’s First COVID-19 DNA vaccine developed in partnership with DBT-BIRAC under Mission COVID Suraksha

- The ZyCoV-D is the world’s first and India’s indigenously developed DNA based vaccine for COVID-19 to be administered in humans including children and adults 12 years and above. This vaccine has been developed in partnership with the Department of Biotechnology (DBT), Government of India under the ‘Mission COVID Suraksha’ and implemented by BIRAC, a PSU of DBT.

- This 3 dose vaccine which when injected produces the spike protein of the SARS-CoV-2 virus and elicits an immune response, which plays a vital role in protection from disease as well as viral clearance.

- Vaccine Technology Centre (VTC), vaccine research centre of the Zydus group, Translational Health Science and Technology Institute (THSTI), an autonomous institute of the DBT and Interactive Research School for Health Affairs (IRSHA), Pune, GCLP Lab set up under the DBT- National Biopharma Mission (NBM) also played a vital role in this success story.

- The plug and play technology on which the plasmid DNA platform is based can be easily adapted to deal with mutations in the virus, such as those already occurring.
What is DNA Vaccine?

DNA Vaccines consist of a plasmid (circular DNA molecule) containing the gene from virus / bacteria, which stimulates the immune system upon delivery.
Currently no DNA vaccines have been approved for use in humans.

But many DNA vaccines are undergoing human clinical trials and some DNA vaccines have been approved by US regulatory agencies.

DNA vaccines in human clinical trials:
- DNA vaccines against cancer
- DNA vaccines against HIV

DNA vaccines approved by United States Food and Drug Administration (FDA) and the United States Department of Agriculture (USDA) for veterinary use:
- Vaccine against West Nile Virus in horses
- Melanoma vaccine for dogs

World’s First COVID-19 DNA Vaccine: The Scientific Journey
DNA Vaccines – Advantages and Challenges

**BENEFITS**

**Stability and Safety**
- DNA Vaccines are non-infectious
- Carries no potential toxicity from viral vectors
- Non-replicating and non-integrating plasmid carrying the gene of interest making it very safe

**Efficacy and Boosting**
- Stimulate both the humoral and cellular arms of the adaptive immune system
- DNA Vaccines pose minimal risk of anti-vector immunity

**Rapid and Scalable Manufacturing**
- Ease of manufacturing related to minimal biosafety requirements (BSL-1)
- Rapid development from concept to human in 5 months
- Improved vaccine stability and lower cold chain requirements

**CHALLENGES**

- Relatively limited data on safety and efficacy in humans
- Risk of development of anti-nuclear antibodies
- Induction of Antibiotic Resistance

World’s First COVID-19 DNA Vaccine: The Scientific Journey
Global COVID-19 Vaccine Landscape

- **112** Vaccines Candidates in Clinical Phase
- **184** Vaccine Candidates in Pre-clinical Development
- **22** Approved Vaccine Candidates

Source: WHO COVID-19 Vaccine Landscape – 20 August 2021

World’s First COVID-19 DNA Vaccine: The Scientific Journey
Major Vaccine Platforms against SARS-CoV-2

- **a. Inactivated vaccines**
  Inactivated vaccines contain SARS-CoV-2 viruses that are chemically inactivated.

- **b. Recombinant proteins vaccines**
  Vaccines composed of recombinant spikes. Viruses-like particles are devoid of genetic material but display spikes, M and E proteins on their surface.

- **c. Viral vector vaccines**
  Viral vector vaccines contain another virus modified to express S protein.

- **d. RNA vaccines**
  RNA vaccines consist of RNA packed in lipid nanoparticles.

- **e. DNA vaccines**
  DNA vaccines contain a circular DNA encoding the spike protein.
DNA Vaccines for COVID-19 – Global Status

Globally 11 DNA Vaccines for COVID-19 are in clinical development

**EUA**
- Zydus Cadila

**Phase II/III**
- Inovio Pharmaceuticals + IVI + Advaccine (Suzhou) Biopharmaceutical Co., Ltd
- AnGes + Takara Bio + Osaka University

**Phase I/II**
- Genexine Consortium
- GeneOne Life Science, Inc.
- Takis + Rottapharm Biotech
- AnGes, Inc

**Phase I/II**
- Entos Pharmaceuticals Inc.
- Providence Health & Services
- Symvivo Corporation
- University of Sydney, Bionet Co., Ltd, Technovalia

Cadila’s ZyCOV-D (India): First DNA vaccine approved for human use

*Source: WHO COVID-19 Vaccine Landscape – 20 August 2021*
Globally 11 DNA Vaccines for COVID-19 are in clinical development 2 vaccine candidates in advanced stage of clinical development Cadila's ZyCOV-D (India): First DNA vaccine approved for human use

<table>
<thead>
<tr>
<th>Type of vaccine candidate</th>
<th>No. of doses</th>
<th>Route of administration</th>
<th>Developer</th>
<th>Current stage</th>
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ZyCoV-D: plasmid DNA based COVID Vaccine: Cadila Healthcare Ltd.

World's first and India's indigenously developed DNA based vaccine for COVID-19

FEATURES OF ZYCOV-D VACCINE

- **Plug and play technology:** The Plasmid DNA platform also allows generating new constructs quickly to deal with mutations in the virus, such as those already occurring.

- **Administration:** Three dose intradermal vaccine: applied using **The PharmaJet® needle free system**, Tropis®, lead to a significant reduction in any kind of side effects

- **Storage:** At 2-8 C but also shows good stability at temperatures of 25 degree C for at least three months

- No problem associated with vector based immunity

- Ease of manufacturing with minimal biosafety requirements (BSL-1)

- **Current Capacity:** 100-120 million doses annually

- Rapid large scale production feasibility

Candidate supported under National Biopharma Mission and Mission COVID Suraksha
ZyCoV-D Vaccine Development and Current Status

- Vaccine stable up to 3 months at 25°C
- Strong immune response in animals and now in humans
- Wild type Virus Neutralization obtained
- No safety concerns

RECEIVED APPROVAL EMERGENCY USE AUTHORIZATION (EUA) FOR CHILDREN AND ADULTS (12 YEARS AND ABOVE) DRUG CONTROLLER GENERAL OF INDIA (DCGI) ON 20TH AUGUST’ 2021
ZYCOV-D Vaccine Clinical Development

- Largest clinical trial > 50 centers (>28000 sample size)
- First COVID-19 vaccine to be tested in adolescent population in the 12-18 years age group in India
- Around 1000 subjects enrolled in 12-18 years age group: vaccine found to be Safe and Very Well Tolerated. The tolerability profile similar to that seen in the adult population.
- Primary efficacy of 66.6% for symptomatic RT-PCR positive cases in the interim analysis.
- No moderate case of COVID-19 disease observed in the vaccine arm post administration of the third dose suggesting 100% efficacy for moderate disease.
- No severe cases or deaths due to COVID-19 in the vaccine arm after administration of the second dose of the vaccine.
- Ease of administration for children: Needle Free (No Risk of needle stick injuries or cross contamination or spread of infection)
- Safe for children: Non-infectious; no potential toxicity from viral vectors
**DBT**
The Department of Biotechnology (DBT), under the Ministry of Science & Technology, promotes and accelerates the development of biotechnology in India, including growth and application of biotechnology in the areas of agriculture, healthcare, animal sciences, environment and industry.

**BIRAC**
Biotechnology Industry Research Assistance Council (BIRAC) is a not-for-profit Section 8, Schedule B, Public Sector Enterprise set up by the Department of Biotechnology (DBT), Government of India. It acts as an Interface Agency to improve and encourage the evolving biotechnology industry to execute strategic research and development activities in context to Nation’s product development needs.

**Zydus Cadila**
Zydus Cadila is an innovative, global pharmaceutical company that discovers, develops, manufactures and markets a broad range of healthcare therapies, including small molecule drugs, biologic therapeutics, and vaccines.