Research & development of vaccines to prevent SARS-CoV-2 infection

Updated September 2020

Disclaimer

No vaccine against COVID-19 is approved. This document does not provide guidance on what vaccine or medicines to take. Please avoid self-prescription and always refer to your doctor before making any treatment decision.

This document provides a selection of updates on the research and development of vaccines for the current coronavirus infection. Those highlights are for the information of patient organisations/groups, advocates and people living with a rare disease. EURORDIS takes reasonable steps to verify the accuracy of the information presented. This document does not constitute, and shall not be deemed or construed as, any approval or endorsement by EURORDIS of such product or entity.
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A ‘must-read’ introduction

This document provides a selection of updates on the research and development of vaccines to prevent SARS-coV2 infection that causes COVID-19. Those highlights are for the information of patient organisations/groups, advocates and people living with a rare disease. EURORDIS takes reasonable steps to verify the accuracy of the information presented. This document does not constitute, and shall not be deemed or construed as, any approval or endorsement by EURORDIS of such product or entity.

EURORDIS has a role in disseminating up-to-date information that could be useful for people living with a rare disease, who are exposed to the SARS-coV2 virus infection. Some rare diseases constitute an aggravated risk when infected by C-19. Some products being studied for C-19 are already approved or used off-label for some rare diseases, with potential information confusion and shortages risks. In other rare diseases, some products being studied for C-19 may have medicinal products interactions with medicines used in the care of these diseases. All good reasons to inform patient advocates with curated though raw information material to empower their respective actions. EURORDIS’s Task Force on Drug Information, Transparency and Access (DITA) was tasked to prepare and regularly update this document. This task force is composed of EURORDIS volunteers and staff.

This document is an editorial selection and highlights the most recent developments for products being currently tested in phase III clinical trials, measuring their efficacy and toxicity. It is by no mean an exhaustive list of all therapeutic research. To avoid repeating the same situation than for the last Ebola outbreak, where the evaluation of potential treatments could not be completed (not enough participants as the trials were started too late), clinical trials against COVID-19 were authorised very soon after the epidemic started. The priority is to enrol participants in authorised trials.

For any questions or clarification, please contact François Houÿez: francois.houyez@eurordis.org
Resources

- EUnetHTA Covid-19 Rolling Collaborative Reviews [https://eunethta.eu/rcr01-rcrxx/](https://eunethta.eu/rcr01-rcrxx/)
- Horizon scanning for treatments and vaccines by the Austrian HTA institute GÖG [https://eprints.aihta.at/1234/](https://eprints.aihta.at/1234/)
- World Health Organization: [https://www.who.int/blueprint/priority-diseases/key-action/Table_of_therapeutics_Appendix_17022020.pdf?ua=1](https://www.who.int/blueprint/priority-diseases/key-action/Table_of_therapeutics_Appendix_17022020.pdf?ua=1)
  All trials for COVID-19: [https://www.who.int/docs/default-source/coronaviruse/covid-19-trials.xls?sfvrsn=a8be2aa0_6&ua=1](https://www.who.int/docs/default-source/coronaviruse/covid-19-trials.xls?sfvrsn=a8be2aa0_6&ua=1)
- The NIH register of clinical trials includes 210 clinical trials to treat COVID-19 (as of 30 March 2020). You can consult here: [https://clinicaltrials.gov](https://clinicaltrials.gov)
  And also
  - A review of the most advanced research was published here in March 2020:
    Research and Development on Therapeutic Agents and Vaccines for COVID-19 and Related Human Coronavirus Diseases. Cynthia Liu et al. ACS Cent. Sci., 315-331. Published 12/03/2020
    [https://pubs.acs.org/doi/10.1021/acscentsci.0c00272](https://pubs.acs.org/doi/10.1021/acscentsci.0c00272)
- Video on the pathophysiology of the virus, the dynamic of the pandemic and how to fight it
  [https://youtu.be/BtNgoy9VOY](https://youtu.be/BtNgoy9VOY)
Vaccines in development

This document is a summary of information on vaccines in development to prevent the SARs-coV2 infection, intended for people living with a rare disease. Sources include the European Medicines Agency and EUnetHTA, the European Network of HTA Agencies that publishes rolling collaborative reviews and horizon scanning reports.

Of all vaccines in development to prevent the infection, the EURORDIS’s Drug Information, Transparency and Access Task Force decided the following selection for its own review:

1. The most advanced vaccine candidates: products in clinical development already, with emphasis on products in phase II, phase II/III and/or phase III.
2. Products with specific issues on efficacy or safety for some groups of rare diseases

Figure 1: https://www.bio.org
Latest news

AztraZeneca vaccine trial RESTARTED

On 8 September 2020, the British-Swedish pharmaceutical company confirmed that one of the volunteers in a UK trial of the vaccine had developed an unexplained illness due to possible adverse reaction in one participant.¹

This is the second time AztraZeneca had to suspend their vaccine trials: there was a brief trial pause in July while a safety review took place after one volunteer was confirmed to have an undiagnosed case of multiple sclerosis, which the independent panel concluded was unrelated to the vaccine.

On September 12th⁴, the U.K. Medicines Health Regulatory Authority recommended that the study resume after an independent review of the safety data triggered a pause on Sept. 6, Oxford said in a statement. It declined to disclose details about the volunteer’s illness.

No announcement was made on the status of trials outside the U.K. Trials were underway in the U.S., Brazil, South Africa and India before being paused after the safety review.

Oxford said some 18,000 people have received “study vaccines” as part of the trials. The trial started just as rates of infection in the U.K. began dropping in May, making it harder to demonstrate whether the vaccine works.

Response from 9 companies to US President for the development of a vaccine

"We, the undersigned biopharmaceutical companies, want to make clear our on-going commitment to developing and testing potential vaccines for COVID-19 in accordance with high ethical standards and sound scientific principles". The industry promise to stick to scientific principles and keep politics out of the approval process comes after President Donald Trump emphasized that a vaccine would likely be ready for public use before the Nov. 3 election.²

All nine companies are individually or jointly developing a candidate COVID-19 vaccine supported at least in part with federal dollars, which so far amounts to more than $10 billion (AstraZeneca, Johnson & Johnson, Moderna Inc., Novavax Inc., Merck, Sanofi and GlaxoSmithKline, and Pfizer Inc., BioNTech).

# Vaccine platforms

<table>
<thead>
<tr>
<th>Platform</th>
<th>Description</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactivated</td>
<td>Whole virus, killed (heated or chemically). It cannot cause illness. In general, inactivated viruses do not provide as strong immune response as an attenuated virus vaccine, so repetition of doses needed</td>
<td>Polio virus influenza</td>
</tr>
<tr>
<td>Live attenuated</td>
<td>Live attenuated vaccines are made up of whole viruses that have been weakened in a lab (usually through culturing). In general, stronger immune response than inactivated vaccines</td>
<td>Tuberculosis, Varicella, MMR (Measles, mumps, rubella), Influenza</td>
</tr>
<tr>
<td>Subunit</td>
<td>Fragment or portion of the virus introduced into the body. This fragment is enough to be recognised by the immune response and stimulate immunity</td>
<td>Pertussis, HPV, Hep. B</td>
</tr>
<tr>
<td>Viral vector</td>
<td>Viral vector vaccines insert a gene for a viral protein into another, harmless virus (replicating or non-replicating). This harmless virus then delivers the viral protein to the vaccine recipient, which triggers an immune response.</td>
<td>Ebola, Veterinary vaccines, Recombinant influenza vaccine</td>
</tr>
<tr>
<td>mRNA</td>
<td>Work by introducing an mRNA sequence (the molecule that tells cells what to build) coded for a disease specific antigen. Once this antigen is reproduced within the body, it is recognised and triggers an immune response.</td>
<td>None</td>
</tr>
<tr>
<td>DNA</td>
<td>Work by inserting synthetic DNA of viral gene(s) into small DNA molecules called plasmids. Cells take in the DNA plasmids and follow their instructions to build viral proteins, which are recognised by the immune system, and prepare it to respond to disease exposure.</td>
<td>None</td>
</tr>
</tbody>
</table>
Vaccine pipeline

WHO is tracking 34 candidates in various stages of development. Here are information on the most advanced candidates (phase I-2, phase 2-3 or phase 3) with their estimated completion date (interim analysis will be performed before the end-date).

<table>
<thead>
<tr>
<th>Company</th>
<th>Vaccine</th>
<th>Platform</th>
<th>Phase</th>
<th>Completion date*</th>
<th>Country</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderna</td>
<td>mRNA-1273</td>
<td>RNA</td>
<td>Phase 3</td>
<td>October 2022</td>
<td>USA</td>
<td>NCT04470427</td>
</tr>
<tr>
<td>CansinoBio</td>
<td>Ad5-nCov</td>
<td>Non-replicating viral vector</td>
<td>Phase 2</td>
<td></td>
<td>China</td>
<td></td>
</tr>
<tr>
<td>Inovio</td>
<td>Ino-4800</td>
<td>Synthesised DNA plasmid vaccine</td>
<td>Phase 1</td>
<td></td>
<td>China, South Korea</td>
<td></td>
</tr>
<tr>
<td>Novavax</td>
<td>VLP recombinant nano-protein</td>
<td>Phase 1-2</td>
<td></td>
<td></td>
<td></td>
<td>NCT04368988</td>
</tr>
<tr>
<td>GSK/Dynavax</td>
<td>molecular clamp</td>
<td></td>
<td>Phase 1</td>
<td></td>
<td>Australia</td>
<td></td>
</tr>
<tr>
<td>CureVac</td>
<td>CVnCoV</td>
<td>mRNA-based vaccine</td>
<td>Phase 1</td>
<td></td>
<td>Belgium, Germany</td>
<td></td>
</tr>
<tr>
<td>BioNTech/Pfizer</td>
<td>BNT-162</td>
<td>mRNA based vaccine</td>
<td>Phase 2-3</td>
<td>November 2022</td>
<td>USA, Germany</td>
<td>NCT04368728</td>
</tr>
<tr>
<td>Sinovac</td>
<td>CoronaVac</td>
<td>Inactivated virus</td>
<td>Phase 3</td>
<td>October 2021</td>
<td>China, Brazil</td>
<td>NCT04456595</td>
</tr>
<tr>
<td>GSK / Sanofi</td>
<td></td>
<td>Recombinant protein, adjuvant</td>
<td>Phase 1-2</td>
<td></td>
<td>USA</td>
<td></td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>ChadOx1nCov-19</td>
<td>Non-replicating viral vector</td>
<td>Phase 3</td>
<td>August 2021</td>
<td>GBR</td>
<td>NCT04400838</td>
</tr>
<tr>
<td>Shenzen Inst.</td>
<td>LV-SMENP-Dc</td>
<td>Lentivirus</td>
<td>Phase 1-2</td>
<td></td>
<td>China</td>
<td></td>
</tr>
<tr>
<td>Research</td>
<td>BCG vaccine</td>
<td>Live attenuated</td>
<td>Phase 2-3</td>
<td>April 2021</td>
<td>Netherlands</td>
<td>NCT04328441</td>
</tr>
<tr>
<td>Murdoch CRI</td>
<td>BCG vaccine</td>
<td>Live attenuated</td>
<td>Phase 2-3</td>
<td>June 2021 or March 2022</td>
<td>Australia</td>
<td>NCT04327206</td>
</tr>
<tr>
<td>Sinopharm</td>
<td>Vero-Cell</td>
<td>Inactivated virus</td>
<td>Phase 3</td>
<td>July 2021</td>
<td>China</td>
<td>ChiCTR2000034780</td>
</tr>
<tr>
<td>Gamaleya</td>
<td>Gam-COVID-Vac</td>
<td>viral two-vector vaccine (sputnik v)</td>
<td>Phase 1-2</td>
<td></td>
<td>Russia</td>
<td></td>
</tr>
</tbody>
</table>
Modern mRNA-1273 vaccine candidate developed by ModernaTX, Inc. in collaboration with NIAID is an encapsulated mRNA-based vaccine (mRNA-1273). It is intended for the prevention of infection through a protein of SARS-CoV-2 that is the key into the human cell. An mRNA-based virus has not been approved for use in humans yet. It is a synthetic RNA strand designed to elicit an immune-response to produce antibodies against SARS-CoV2.

To learn more on mRNA vaccines and how they were discovered, an informative video by the NIH Vaccine Research Centre here: [https://www.youtube.com/watch?v=uXcA-mByGfw&feature=youtu.be](https://www.youtube.com/watch?v=uXcA-mByGfw&feature=youtu.be)

**Development phase**

Currently, there is a phase 1 trial with 45 healthy participants (NCT04283461). It takes place in three centres in the US where the participants are split to 3 groups where they receive two injections of low, medium or high doses of mRNA-1273.

Results: After the second vaccination, serum neutralising activity was detected by two methods in all participants evaluated, with values generally similar to those in the upper half of the distribution of a panel of control convalescent serum specimens.

Moderna finalised the phase 3 protocol based on feedback from the U.S. Food and Drug Administration (FDA). The trial is currently ongoing (NCT04470427):

- **Design:** randomised to 1:1 placebo-controlled trial
- **Enrolment:** approximately 30,000 participants enrolled in the U.S
- **Dose:** the 100 μg dose level was chosen as the optimal dose level, based on the results of the Phase 1 study. As of 17 August 2020, a preliminary report with the results from the above-mentioned phase 1 study was published.

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- Interim analysis: possibly after the first 10,000 participants are recruited, depending on the occurrence of events (infections), not before mid-November 2020

CansinoBio

Developer

CanSino Biologics Inc. and the Beijing Institute of Biotechnology

Description

The AD5-nCoV vaccine candidate is a replication-defective adenovirus type 5 (viral vector) that expresses SARS-CoV-2 spike proteins (antigens). The platform (non-replicating viral vector) of AD5-nCoV was originally used for an Ebola vaccine (time to market minus 3 years).

Development phase

The first clinical phase 1 trial (ChiCTR2000030906/NCT04313127) with 108 healthy adults is a single-centre dose-escalation study to test both the safety and tolerability of AD5-nCoV injections in three intervention groups using different dosages (low, medium and high). Specific T-cell response peaked at day 14 post-vaccination. (See results)⁴

As of 17 August, 2020 the results from the a phase 2 RCT were published:⁵

Both doses of the vaccine induced significant neutralising antibody responses to live SARS-CoV-2.

Severe adverse reactions were reported by 24 (9%) participants in the 1 ×10¹¹ viral particles dose group and one (1%) participant in the 5 ×10¹⁰ viral particles dose group. No serious adverse reactions were documented. Authors concluded that the Ad5 vectored COVID-19 vaccine at 5 ×10¹⁰ viral particles is safe, and induced significant immune responses in the majority of recipients after a single immunisation.


Inovio Ino-4800

Developer

Inovio Pharmaceuticals Inc.

Description

Ino-4800 is a DNA plasmid vaccine based on a DNA platform. The DNA is hereby synthesised in a laboratory, hence, no actual virus samples are required. The company’s DNA platform was previously utilised for a MERS-CoV vaccine (INO-4700) tested in a phase I trial.

Development phase

A phase 1 clinical trial started in April 2020. The results are aimed to be presented and published later (April 2021).

The phase 1, non-randomised, open-label, sequential assignment clinical trial (NCT04336410) in 40 healthy adult volunteers aims to evaluate the safety, tolerability and immunological profile of INO-4800 administered by intradermal (ID) injection followed by electroporation (EP) using CELLECTRA® 2000 device.

Phase 1/2 trial (NCT04447781) aims to evaluate the safety, tolerability and immunological profile of INO-4800 administered by intradermal (ID) injection followed by electroporation (EP) using the CELLECTRA® 2000 device in 160 healthy adults aged 19 to 64 years in Republic of K

To date, no completed studies in humans are available for the INO-4800 vaccine candidate.
Novavax

Developer

Novavax and co-sponsored by Coalition for Epidemic Preparedness Innovations (CEPI)

Description

Recombinant protein nanoparticle technology platform that is to generate antigens derived from the coronavirus spike (S) protein. Novavax also expects to utilise its proprietary Matrix-M™ adjuvant in order to enhance immune responses.

Development phase

Novavax initiated a Phase 1/2 clinical trial in May/June 2020. Novavax has previous experience with both MERS and SARS.

The phase 1/2, randomised, placebo-controlled, triple-blind, parallel assignment clinical trial (NCT04368988) in 131 healthy adults aims to evaluate the immunogenicity and safety of SARS-CoV-2 rS nanoparticle vaccine with or without Matrix-M adjuvant in healthy participants ≥ 18 to 59 years of age.

An interim analysis of Part 1 safety and immunogenicity data will be performed prior to an optional expansion to Part 2.

To date, no completed studies in humans are available for Novavax COVID-19 vaccine.
GSK / Dynavax

Developer

Dynavax, Glaxo Smith Kline and the University of Queensland.

Description

The potential vaccine uses a molecular clamp stabilised Spike proteins. The so-called ‘molecular clamp’ technology is intended to prevent infection by synthesising surface proteins and "clamping" them into shape. In so doing, the immune system may induce a response, by recognising them as the correct antigen on the surface of the virus, more easily.

Initially, this technology was designed to be a platform for generating vaccines against different viruses such as influenza, Ebola, and the MERS coronavirus.

Development phase

A Phase 1 randomised, double blind, placebo-controlled, dosage-escalation trial started on July 13, 2020 (ACTRN12620000674932/NCT04495933). The estimated study completion date is September 2021.

To date, no completed studies in humans are available for the candidate vaccine.

CureVax

Description

A protamine-complexed mRNA-based vaccine expressing undisclosed SARS-CoV-2 protein(s). This means that CureVac’s technology uses mRNA as a data carrier in order to train the human body to produce ideal levels of proteins. Thereby the immune system is stimulated and can respond to antigens.

Development phase

Phase 1 (NCT04449276) study aims to evaluate the safety and reacto-genicity profile after 1 and 2 dose administrations of CVnCoV at different dose levels.
AztraZeneca vaccine RESTARTED

On 8 September 2020, the British-Swedish pharmaceutical company confirmed that one of the volunteers in a UK trial of the vaccine had developed an unexplained illness due to possible adverse reaction in one participant.6

All trials of this vaccine, which have so far included at least 17,000 people across the UK, Brazil and South Africa, have been halted.

This is the second time: there was a brief trial pause in July while a safety review took place after one volunteer was confirmed to have an undiagnosed case of multiple sclerosis, which the independent panel concluded was unrelated to the vaccine.

On September 12th, the U.K. Medicines Health Regulatory Authority recommended that the study resume after an independent review of the safety data triggered a pause on Sept. 6, Oxford said in a statement. It declined to disclose details about the volunteer’s illness.

No announcement was made on the status of trials outside the U.K. Trials were underway in the U.S., Brazil, South Africa and India before being paused after the safety review.

Oxford said some 18,000 people have received “study vaccines” as part of the trials. The trial started just as rates of infection in the U.K. began dropping in May, making it harder to demonstrate whether the vaccine works.

Developer

The ChAdOx1 nCoV-19 (AZD1222) is developed by AstraZeneca, licensed from Oxford University) vaccine candidate developed by the Jenner Institute at Oxford University.

Description

It is based on a non-replicating viral vector. A chimpanzee adenovirus platform is hereby used. This platform was previously utilised in clinical phase I trials for a vaccine against MERS.

The vaccine candidate uses a genetically modified safe adenovirus that may cause a cold-like illness. The intended prevention is through the modified adenovirus producing Spike proteins, eventually leading to the formation of antibodies to the coronavirus’s Spike proteins.

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Development phase

Currently, the first clinical phase 1/2 trial in 510 healthy adults is ongoing (ISRCTN 15281137).

Primary endpoints are measured within six months and an optional follow-up visit is offered at day 364. The study is estimated to be completed in May 2021.

In parallel, a Phase 2b/3 study (EUdraCT 2020-001228-32/NCT04400838) is ongoing, to determine the efficacy, safety and immunogenicity of ChAdOx1 nCoV-19. The primary endpoint is virologically confirmed (PCR positive) symptomatic COVID-19 infection.

A Phase 3 RCT (ISRCTN89991424) started in Brazil and South Africa, with another country in Africa set to follow, as well as a trial in the US. Participants are randomly allocated to receive the investigational vaccine or a well-established meningitis vaccine. The study is estimated to be completed in July 2021.

Completion: August 20201. Interim analysis before, but completion needed for statistical power to analyse all 11 subgroups.

Exclusion criteria

Many rare conditions are not compatible with the inclusion in this trial (it is a phase 2b/3, with intense toxicity monitoring).

Results

As of 17 August, 2020, a preliminary report with the results from the phase 1/2 single-blind, RCT (ISRCTN 15281137/NCT04324606/EudraCT 2020-001072-15) was published. 1,077 participants were enrolled and assigned to receive either ChAdOx1 nCoV-19 (n=543) or MenACWY (n=534), ten of whom were enrolled in the non-randomised ChAdOx1 nCoV-19 prime-boost group.

There were no serious adverse events.

In the ChAdOx1 nCoV-19 group, spike-specific T-cell responses peaked on day 14. Anti-spike IgG responses rose by day 28 and were boosted following a second dose.

Authors concluded that ChAdOx1 nCoV-19 showed an acceptable safety profile, and homologous boosting increased antibody responses and together with the induction of both humoral and cellular immune responses, support largescale evaluation of this candidate vaccine in an ongoing phase 3 programme.

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BioNTech

Developer

Developed by BioNTech in collaboration with Fosun Pharma and Pfizer

Description

mRNA platform-based vaccine expressing codon-optimized undisclosed SARS-CoV-2 protein(s)

Development phase

BNT-162 entered clinical testing by the end of April 2020 and R&D is supposed to be carried out both in the US and in Germany. This is a phase 1/2, randomised, placebo-controlled, triple-blind, dose-finding, and vaccine candidate-selection study in healthy adults (NCT04368728/EudraCT 2020-001038-36).

Phase 2/3 RCT has started also (NCT04368728/EudraCT 2020-002641-42) with aim to describe the safety, tolerability, immunogenicity and efficacy of BNT-162. The estimated number of participants is 29481, and completion study date November 2022.

To date, no completed studies in humans are available for the BNT-162 vaccine.

SinoVac

Developer

The private Chinese biopharmaceutical company Sinovac Biotech Ltd.

Description

CoronaVac, an inactivated COVID-19 vaccine candidate.
Development phase

The phase 1 and 2 trials started on April 16, 2020 in Jiangsu Province, China.

According to Sinovac announcement, preliminary phase I/II results showed that there was no serious adverse event after vaccinating a total of 743 volunteers. 90% seroconversion was observed in the phase II clinical trial 14 days after completion of a two-dose vaccination at day 0 and day 14.

A Phase II study on elderly adults is being conducted which will be followed by child and adolescent groups. The phase II trial is expected to be completed at the end of 2020.

Sinovac registered a new Phase 3 RCT (NCT04456595), aiming at assessing efficacy and safety of the Adsorbed COVID-19 (inactivated) vaccine in health care professionals in Brazil. Estimated number of participants is 8,870.

Interim preliminary efficacy analysis can be triggered by reaching the target number of 150 cases. The study is estimated to be completed in October 2021.

China National Pharmaceutical Group Corporation (SINOPHARM)

Developer

Sinopharm is a state-owned Chinese company

Description

Vero-Cell is a β-propiolactone–inactivated whole-virus vaccine against COVID-19.

Development phase

A phase 3 double-blind, placebo controlled RCT has been initiated (ChiCTR2000034780), to evaluate the protective efficacy of inactivated SARS-CoV-2 Vaccine (Vero Cell) after full course of immunisation in healthy subjects aged 18 years old and above. The study is estimated to be completed in July 2021.
Sanofi-GSK

Developer
Sanofi developers a recombinant protein (technology already use for a flu vaccine) while GSK provides an adjuvant.

Development phase
A phase 1-2 randomised, double-blinded, placebo controlled trial is in progress with 440 participants (NCT04537208), recruiting in the USA only.
A phase 3 trial could be submitted end 2020.

BCG Vaccine

Developer
Two research groups, one in the Netherlands, and one in Australia.

Description
Live attenuated virus: repurposing the BCG vaccine, originally for tuberculosis, to fight SARS-CoV2 in healthcare workers at high risk.

Development phase
RCTs in Netherlands (BCG-CORONA phase 3 trial, NCT04328441) and Australia (BRACE phase 3 trial, NCT04327206) aim to assess whether BCG-Danish reduces the incidence and severity of COVID-19 in health-care workers, and the effect this has on days off work.
1,000 healthcare professionals to be enrolled in 8 hospitals to receive the vaccine or placebo.
Sputnik V Vaccine (Russia)

This Russian COVID-19 vaccine Sputnik V is the first in the world with a national authorisation for human use. It was approved for public use even ahead of its Phase III trial. No trial data are published.

Developer

Gamaleya Research Institute of Epidemiology and Microbiology,

Description

Gam-COVID-Vac is a viral two-vector vaccine based on the human adenovirus, a common cold virus, fused with the spike protein of SARS-CoV-2 to stimulate an immune response.

Development phase

Sputnik V is approved for distribution in Russia, despite having been tested only in a small number of people in early-stage clinical trials that lasted two months, normally a process requiring a year or more of clinical assessment for proof of vaccine safety and efficacy against viral disease. In fact, no phase 3 trial has started as of September 2020.

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8 "Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia". The Lancet: 1–11. 4 September 2020. doi:10.1016/S0140-6736(20)31866-3.
Initiatives of interest
Vaccine trials and initiatives

COVID-19 Prevention Trial Network (COVPN)

NIAID established a new clinical trials network - The COVID-19 Prevention Trials Network (COVPN), that aims to enroll thousands of volunteers in large-scale clinical trials testing a variety of investigational vaccines and monoclonal antibodies intended to protect people from COVID-19.

The first Phase 3 clinical trial that the COVPN is expected to conduct with the investigational mRNA-1273 vaccine, developed by NIAID scientists and their collaborators at Moderna, Inc., based in Cambridge, Massachusetts.⁹

ACCESS (vACcine Covid-19 monitoring ReadinESS)

Utrecht scientists (in close collaboration with RIVM, Netherlands Pharmacovigilance centre LAREB and the PHARMO Institute in the Netherlands) are leading an European project with the aim to create an infrastructure and to prepare European organisations to collaboratively evaluate the benefits, coverage and risks of the novel COVID-19 vaccines in their post-licensure phase. The project is funded by the European Medicines Agency (EMA).¹⁰

COVAX

The COVAX initiative consists in purchasing distributing fairly two billion vaccine doses in 2021. It emerged from the World Health Organization (WHO), the Coalition for Epidemic Preparedness Innovations (CEPI) and from GAVI, the Vaccine Alliance.

NIAID Vaccine Research Centre

Almost of developments of SARS-coV2 vaccines derive from research for an HIV vaccine.\textsuperscript{11}

\textsuperscript{11} Barney Graham, Deputy Director, Vaccine Research Centre
### Cheat Sheet: COVID-19 vaccine pipeline

<table>
<thead>
<tr>
<th><strong>Primary sponsor(s)</strong></th>
<th><strong>Description</strong></th>
<th><strong>Platform</strong></th>
<th><strong>Funders</strong></th>
<th><strong>Status</strong></th>
<th><strong>Considerations</strong></th>
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</table>
| **Oxford/AstraZeneca** | ChAdOx1 nCoV-17 vaccine vector expressing SARS-CoV-2 spike protein | viral vector | USS 31,280 | F1: initially 1000 vials/K F1: FIA approved F1, 10,000 vials F1, 200,000 vials | Immunogenicity: Preliminary Ph. IIA data showed both antibody and T-cell responses. Not structured delivery: AstraZeneca vector vaccine could potentially be manufactured quickly at scale (capacity to produce 20 doses has already been secured). Platform stability: No AstraZeneca vector vaccines are currently licensed for use in humans. | Sourced |**
| **Moderna** | mRNA-1273 Synthetic messenger RNA 28-mer oligonucleotide for SARS-CoV-2 spike protein | mRNA | USS 3,950M | F1: I, ongoing; 155 vaccinations + 116 placebo | Immunogenicity: Ph. I data showed that a single dose with more than 90% efficacy was observed in patients who had recovered from COVID-19. Not a structured delivery: mRNA vaccines were developed to scale and manufactured (pilot for 18 doses by 2020, likely to require two doses, but a third may be necessary). Platform stability: No mRNA vaccines are approved for use in humans. | Moderna Statement |**
| **Inovio** | INO-4800 DNA plasmid vaccine with electroporation | DNA | USS 51.7M | F1: ongoing: 40-volts | Immunogenicity: Preclinical data showed antibody and cell-mediated immune responses. Not a structured delivery: INO-4800 is stable at room temperature for more than a year and is not refrigerated to be stored or transported. Platform stability: No DNA vaccines are approved for use in humans. | Inovio Ph. 1 Statement |**
| **Novavax** | NVX-CoV2373 Full-length recombinant SARS-CoV-2 glycoprotein administered with Matrix-M | Protein Subunit | USS 14.9M | F1: World Health Organization (WHO) phase IIb trial completed; F1, 1 phase III trial planned | Immunogenicity: Ph. I data showed both antibody and T-cell responses. Not a structured delivery: GMP production carried out with capacity for large-scale manufacturing (25,16 doses by end of 2021). Platform stability: The same nanoparticle platform successfully used in Ph. I trials for Novavax’s seasonal influenza vaccine for older adults. | Novavax Statement |**
| **J&J** | ad5261SARS-CoV-2 Adenovirus vector expressing SARS-CoV-2 spike protein | viral vector | J&J investment (~$300M) | F1: Ph. II ongoing: 150-volts US and Belgium F1, 1 phase II trial planned: 180-volts | Immunogenicity: Preliminary data shows that a single dose may be all that is needed, the potential for persisting immunity against SARS-CoV-2. Not a structured delivery: TEC. Platform stability: J&J uses the same technology to make its Ebola vaccine, which was granted European Medicines Agency approval in May 2020. | J&J |**
| **Merck** | SARS-CoV-2 Spike Protein vectored vaccine | viral vector | US$ 238M | Preclinical | Immunogenicity: TEC, though replicative viral vectors potentially lead to robust immune responses triggered by a single dose. Manufacturing delivery: TEC. Platform stability: Use of established vaccine technology (Ebola) could speed development. | Merck |**
| **Pfizer/BioNTech** | BNT162b2 mRNA vaccine expressing SARS-CoV-2 Spike protein | mRNA (L4) | Pfizer ($500M) USS 65.5M | F1: FIA approved F1, 1 phase IIb/III trial completed | Immunogenicity: Ph. I data show both neutralizing antibody and T-cell responses. Manufacturing delivery: mRNA vaccines are relatively easy to scale and manufacture. Platform stability: No licensed mRNA vaccines. | Pfizer-BioNTech Yen |**
| **Imperial College London** | SARS-CoV-2 S episomal DNA vaccine expressing SARS-CoV-2 spike protein | SARS-CoV-2 Spike DNA | UK ($40M) Fhla I Immunotherapeutics ($2.9M) | F1: Ph. I ongoing; 150-volts UK F1, 1 phase I trial planned: 300-volts | Immunogenicity: TEC. Manufacturing delivery: Imperial College and a special-purpose company to sell the vaccine (Masterly) to be financed by UK and Gavi. Platform stability: No licensed SARS-CoV-2 DNA vaccines. | Imperial College London Yen |**
| **CureVac** | mRNA vaccine that expresses the SARS-CoV-2 spike proteins transformed with live naked particles | mRNA | CEP ($83.9M) Biz ($25M) USS ($120M) | F1: I ongoing: 160/Germany, Belgium | Immunogenicity: TEC. Manufacturing delivery: mRNA vaccines are relatively easy to scale and manufacture. Platform stability: No licensed mRNA vaccines. | CureVac Statement |
### Vaccine Pipeline

<table>
<thead>
<tr>
<th>Sponsor(s)</th>
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<tbody>
<tr>
<td>Sinovac Biotech</td>
<td>A-S-SWIM: Antibody response SARS-CoV-2 spike protein</td>
<td>Ideal</td>
<td>No funding disclosed.</td>
<td>Pl. 1 completed; 286 with China; published</td>
<td>Immunogenicity: Pl. 1 participants developed binding antibodies, neutralizing antibodies and T-cell responses, potential for preventing immunity against SARS-CoV-2. Manufacturing: 80m doses by year-end. FDA to list as a &quot;special needed drug&quot;.</td>
<td>Sponsored Press Release</td>
</tr>
<tr>
<td>Clover BioPharma</td>
<td>SARS-CoV-2</td>
<td>Subunit</td>
<td>CEPI ($2.5M)</td>
<td>Pl. 1 ongoing; 190k vaccine Pl. 2 planned.</td>
<td>Immunogenicity, in preclinical studies, inactivated SARS-CoV-2 induced neutralising antibodies in a macaque model. Manufacturing: Affinity. The adjuvant system is designed to boost the immune response and was tested in preclinical studies for the manufacturer's influenza SARS-CoV-2 vaccine candidate.</td>
<td>Press release</td>
</tr>
<tr>
<td>Sanofi</td>
<td>3D9 virus surface proteins of the SARS-CoV-2 virus expressed in insect cells, which express a antigen that is then purified and covalently linked to 2015 influenza A/US9 a vaccine.</td>
<td>Subunit</td>
<td>IESC 2019</td>
<td>Pl. 1: LV plasmid, Sep. 2020; Pl. 2: IESC 321 (Nov 2020)</td>
<td>Immunogenicity: TCD, manufacturing capacity. The adjuvant system is designed to boost the immune response and was tested in preclinical studies, with the following drug doses to be supplied: SARS-CoV-2 vaccine: 80m doses of the adjuvant system in 2021. Platform to help with in-licensed technologies.</td>
<td>Sponsored Statement</td>
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The COVID-19 vaccine pipeline Cheat Sheet reflects front-runner candidates along with products with significant investments from the US, CEPI, and the WHO.

### Vaccine Platforms

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<tr>
<th>Platform</th>
<th>About</th>
<th>Licensed Products</th>
<th>Learn more</th>
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<tbody>
<tr>
<td>Inactivated</td>
<td>Inactivated vaccines consist of the whole virus, which has been killed with heat or chemicals so that it can't cause illness. In general, inactivated vaccines provide a strong immune response to inactivated vaccines, so additional doses may be needed.</td>
<td>Polia</td>
<td>Inactivated inactivated vaccines</td>
</tr>
<tr>
<td>Live Attenuated</td>
<td>Live attenuated vaccines are made up of whole viruses that have been weakened in lab (usually through culturing). They tend to elicit a stronger immune response than inactivated vaccines.</td>
<td>MNV, Varicella, TIV</td>
<td>Live attenuated vaccines: historical vaccines and current challenges</td>
</tr>
<tr>
<td>Subunit</td>
<td>Subunit vaccines introduce a fragment or portion of the virus into the body. This fragment is less likely to be recognized by the immune system and stimulate antibodies.</td>
<td>Polio, Hepatitis B</td>
<td>Subunit Vaccines</td>
</tr>
<tr>
<td>Wool vector</td>
<td>Wool vector vaccines insert a gene from viral proteins into a vector, which mimics immunity (i.e., simulating or mimicking). These vaccines then deliver the viral proteins to the vaccine recipient, which triggers an immune response.</td>
<td>Ebola, Malaria vaccine</td>
<td>What are viral vaccines?</td>
</tr>
<tr>
<td>mRNA</td>
<td>mRNA vaccines work by instructing an mRNA sequence to the cells that tell the cell to be mRNA coded for a coronavirus-specific antigen. Once this antigen is expressed within the body, it is recognized and triggers an immune response.</td>
<td>None</td>
<td>An introduction to mRNA vaccines</td>
</tr>
<tr>
<td>DNA</td>
<td>DNA-based vaccines work by inserting the genetic DNA of a virus into a gene expression system called plasmids. Cells take the DNA plasmids and follow their instructions to build viral proteins, which are recognized by the immune system and produce a response.</td>
<td>None</td>
<td>DNA-based vaccine</td>
</tr>
</tbody>
</table>

*Operation Warp Speed: US government body responsible for strategic approach, coordination and resource allocations for COVID-19 vaccines
**COVAX: The vaccine pillar of ACT-A, the global collaboration to accelerate development, production and equitable access to new diagnostics, therapeutics and vaccines. COVAX is led by GAVI, CEPI and WHO.

### About RVAC

RVAC is a non-profit organization that uses education, policy analysis, advocacy and a network of global collaborations to accelerate the ethical development and global delivery of new HIV prevention options as part of a comprehensive response to the pandemic. For more information, visit [www.rvac.org](http://www.rvac.org)