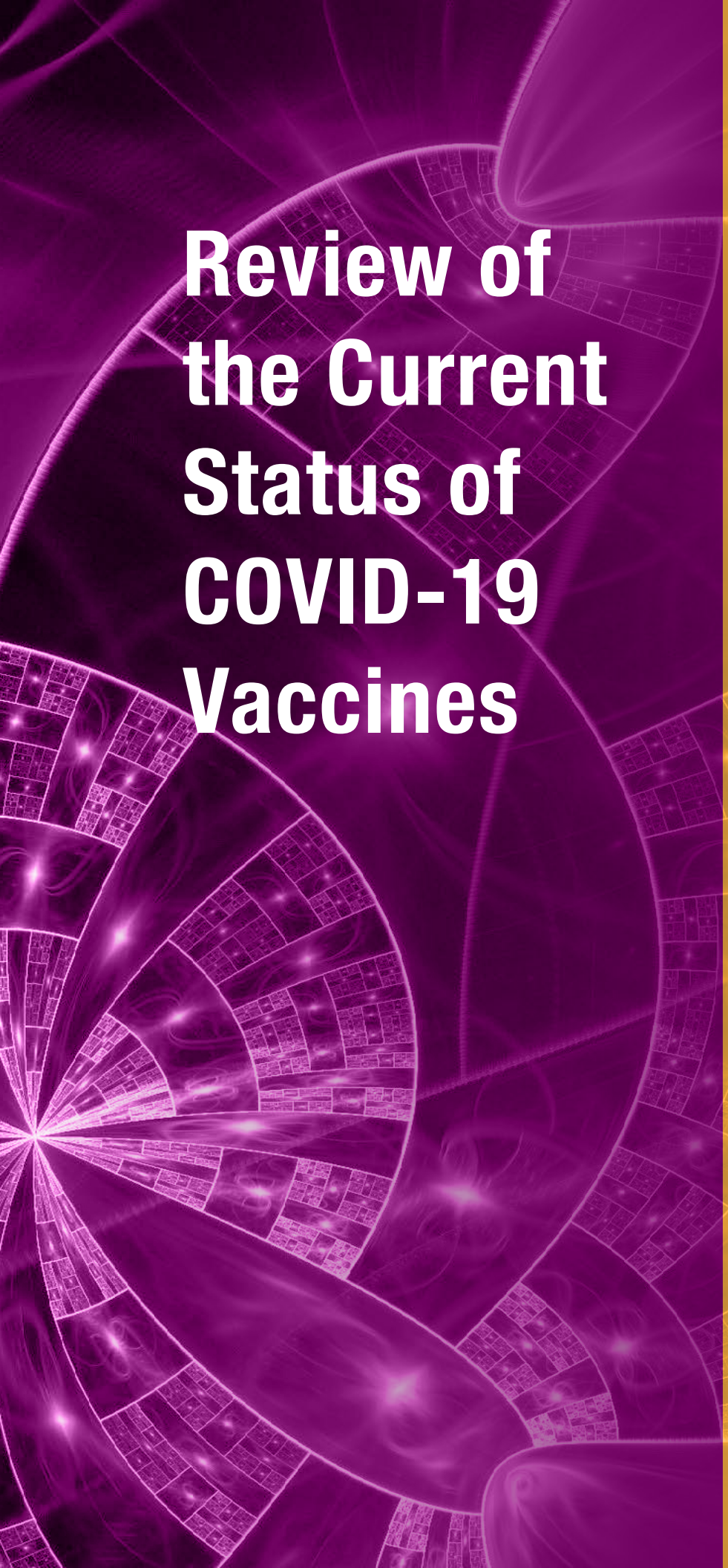
Review of the Current Status of COVID-19 Vaccines



A Report by the
UWI-STA Committee
on Vaccine Efficacy

December 2020

UWI-STA Committee on Vaccine Efficacy
Faculty of Medical Sciences
The University of the West Indies
St. Augustine Campus
Trinidad and Tobago, W.I.
Tel (868) 645-3232 ext 5026
Fax (868) 663-9836

December 2020

Preface

We must commend the Faculty of Medical Sciences ad hoc committee on vaccines for the thorough job they have done in reviewing the current data available in the public domain on vaccines. When the Ministry of Health appointed its vaccines committee in early December 2020, we recognized the direct need for a summary of the latest information available in this area and that we did not have much time to do it more so with the Christmas break around the corner. All departments and schools of The Faculty were involved as well as The Caribbean Centre for Health Systems Research and Development. Indeed, this committee responded magnificently to the task and on behalf of The Faculty I would like to thank Prof Clement and his team for the work done here.

Terence Seemungal
Dean
Faculty of Medical Sciences
The University of the West Indies
St. Augustine Campus

Foreword

The Ministry of Health and the Faculty of Medical Sciences at St. Augustine are to be commended for collaborating at speed to consider the state of vaccine development and factors that will determine the outcome of the COVID-19 vaccination campaign in Trinidad and Tobago. This report from the UWI-STA Committee on Vaccine Efficacy helps build the scientific evidence base for policymakers - in Trinidad and Tobago and the wider Caribbean - to make informed decisions on vaccine procurement, uptake and roll-out. The report highlights both the successes of vaccine manufacturers in developing safe and effective vaccines within such a short time period but also identifies the challenges likely ahead due to the logistics of administering two-shot vaccines, maintaining cold-chain requirements and facing up to "anti-vaxx" sentiment and misinformation that is fueling vaccine hesitancy among Caribbean populations. By drafting this scientific report at such short notice, members of the UWI-STA Committee on Vaccine Efficacy are embodying the public service ethos of UWI that is most keenly appreciated at times of national emergency. The report interfaces with other academic outputs created by the UWI COVID-19 Task Force (www.uwi.edu/covid19) as a part of UWI's remit to serve as a public academy for the Caribbean region.

Clive Landis
Pro-Vice Chancellor for Undergraduate Studies &
Chair, UWI COVID-19 Taskforce

UWI-STA Committee on Vaccine Efficacy
Committee Members and Objectives

Committee Members	Designation
Dr Carla-Maria Alexander	Lecturer, Immunology, School Of Medicine
Professor Yuri Clement (Chairman)	Professor, Pharmacology, School Of Medicine
Dr Maritza Fernandes	Lecturer, Paediatrics, School Of Medicine
Dr Stanley Giddings	Lecturer, Medicine (Infectious Diseases), School Of Medicine
Ms Shelly-Ann Hunte	Research Fellow, Centre For Health Systems Research And Development
Dr Diane Ignacio	Lecturer, School Of Pharmacy
Ms Marsha Ivey	Lecturer, Public Health & Primary Care Unit, School Of Medicine
Dr Satish Jankie	Lecturer, School Of Pharmacy
Professor Michele Monteil	Professor, Immunology
Dr Philip Onuoha	Senior Lecturer, School Of Nursing
Dr Shalini Pooransingh	Lecturer, Public Health & Primary Care Unit, School Of Medicine
Ms Avril E. Reid	Head, Medical Sciences Library
Mrs Shurla Sampson-Francis	Senior Administrative Assistant,School Of Medicine
(listed alphabetically by surnames)	

Objectives

The Committee was guided by the following objectives:

1. To research the current status of all COVID-19 vaccines in use or development as listed in the WHO landscape of COVID-19 vaccines, 10 December 2020.
2. To provide critical assessment of vaccines currently in use, BioNTech/Pfizer and Moderna mRNA vaccines, specifically:
   a. Efficacy – overall and in different sub-populations;
   b. Adverse event profile;
   c. Duration of protection;
   d. Delivery and storage requirements; and
   e. Any other relevant information gleaned from clinical trials and post-immunization surveillance.
3. To provide an update of clinical trials, from available published data, on vaccines in current Phase III trials and with anticipated USA Federal Drug Administration (FDA) Emergency Use Authorization in the near future, e.g. Astra Zeneca viral vector vaccine.
4. To summarize the current status of all other vaccines in development from available and reliable sources of data.

Contents

Contents

Abbreviations

AE	Adverse Events
ADEM	Acute Disseminated Encephalomyelitis
BMI	Body Mass Index
CD	Cluster of Differentiation
CDC	Centers for Disease Control and Prevention
CITAG	Caribbean Immunization Technical Advisory Group
COVID-19	Coronavirus Disease
DNA	Deoxyribonucleic Acid
ELISA	Enzyme-Linked Immunosorbent Assay
FDA	Food and Drugs Administration
Hep B	Hepatitis B
Hep C	Hepatitis C
HIV	Human Immunodeficiency Virus
ICU	Intensive Care Unit
IFN-γ	Interferon Gamma
im	Intramuscular
LD	Low Dose
GMT	Geometric Mean Titre
MIS-C	Multisystem Inflammatory Syndrome in Children
mRNA	Messenger RNA
NP	Nasopharyngeal
PAHO	Pan American Health Organization
rAds	Recombinant Human Adenovirus
RBD	Receptor Binding Domain
RNA	Ribonucleic Acid
RT-PCR	Reverse Transcriptase - Polymerase Chain Reaction
SAE	Serious Adverse Events
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SD	Standard Dose
VE	Vaccine Efficacy
WHO	World Health Organization

Executive Summary

On 11th December 2020, Professor Terence Seemungal (Dean, Faculty of Medicine) appointed an ad-hoc UWI-STA Committee on Vaccine Efficacy to assess the clinical evidence for COVID-19 vaccines in current use and in ongoing clinical trials. The report is intended for use by the National Immunization Technical Advisory Group of Trinidad and Tobago (NITAG).

Vaccines for review were selected from the World Health Organization's list of COVID-19 candidate vaccines from eight types (platforms) published on 10th December 2020. Selected vaccines were in different phases of clinical development. The aim of the Committee was to explore the range of vaccine types and summarize what is known about their efficacy, safety, quality and duration of host immunity, delivery and storage requirements, and any other relevant information from the ongoing trials and post-immunization surveillance.

The Committee identified published reports and other documentation following database searches in PubMed (MEDLINE), ClinicalTrials.gov, WHO International Clinical Trials Registry, Cochrane Central Registry of Controlled Trials (CENTRAL), Chinese Clinical Trials Registry and other vaccine-related websites.

Details of identified studies were extracted and summarized in a series of narratives arranged by vaccine platforms. The methodological quality of trials was assessed using the Cochrane Risk of Bias tool and an overall grade (very low, low, moderate or high) was assigned. The Committee was interested in outcomes such as prevention, immunogenicity and safety.

The Committee placed special emphasis on vaccines already in use and those expected to obtain Emergency Use Authorization soon in the USA, UK, EU, or elsewhere. Two mRNA vaccines, BioNTech/Pfizer (BNT162b2) and Moderna mRNA 1273, are approved for use in the USA and UK (Pfizer only). These vaccines are delivered in two doses, 21 days (3 weeks) apart for the BioNTech/Pfizer vaccine and 28 days (4 weeks) apart for the Moderna vaccine.
A multi-national Phase 3 clinical trial of the BioNTech/Pfizer vaccine with about 44,000 participants over 16 years old and randomized 1:1 (vaccine to placebo) showed efficacy of 95% [CI: 90.3 - 97.6], with a good safety profile.

The Moderna mRNA 1273 Phase 3 trial conducted at 99 sites in the USA, with about 30,000 participants over 18 years old and randomized 1:1 (vaccine to placebo), showed vaccine efficacy of 95.6% [95% CI: 90.6 – 97.9] for participants less than 65 years old and 86.4% [95% CI: 61.4 – 95.5] for participants over 65 years old.

The question of the ethnic composition of the trial populations in these trials was raised. It was noted that in both mRNA vaccine trials participants of African, Asian and Mixed ancestry comprised 9%, 4% and 2% respectively of the trial populations. It was deemed that vaccine efficacy in these ethnic groups was similar to the overall Moderna and Pfizer study populations.

The recent roll out of immunization with the Pfizer and Moderna vaccines in the UK and USA has identified rare occurrences of anaphylactic-like reactions among vaccinees. Some, but not all, of those exhibiting these rare reactions, were known to have had severe allergies. These idiosyncratic responses are being investigated, but raise the question as to whether individuals with prior anaphylactic/anaphylactoid reactions should receive this type of vaccine. Consequently, it will be important for the Ministry of Health to provide protocols for appropriate identification and management of highly allergic persons requiring COVID-19 vaccination in Trinidad and Tobago.

The University of Oxford/Astra Zeneca (ChAdOx1 nCov-19) viral vector vaccine generates strong humoral and cell-mediated immunity, it is delivered in two doses, with the second dose being given 4 to 12 weeks after the first. Presently, the Oxford/Astra-Zeneca vaccine has two reported efficacies depending on the full or half-dose regime: 62.1 and 90.0%. It does not require ultra-cold storage and can be stored between 2°C and 8°C for up to six months. This vaccine was approved for use in the UK on 30 December 2020.

The approved Russian adenovirus viral vector vaccine (Sputnik V/Gam-COVID-Vac) produced by Gamaleya Research Institute reportedly generates good immune responses. However, there is concern about the quality of the evidence, as it was approved following small Phase 1 and 2 trials, without the benefit of large, well-designed Phase 3 trials to access safety and efficacy. Furthermore, both Phase 1 and 2 trials included mostly young males of one ethnic group and do not provide details about efficacy in other ethnic groups or subpopulations. Similarly, the EpiVacCorona, a protein sub-unit vaccine, was approved for mass vaccination in Russia following small Phase 1 and 2 clinical trials with little data from robust Phase 3 clinical trials.

An approved inactivated whole virus vaccine, BBIBP-CorV, produced by Sinopharm (China) is currently in use in China, the UAE and Bahrain. Although this vaccine was tested in Phase 3 trials in six countries in the Middle East, South America and China, with a reported vaccine efficacy of 86%, there is very little published data to interrogate the evidence.

The Novavax vaccine, a protein subunit vaccine, is currently in large multinational Phase 3 trials. Smaller trials of virus-like particles and DNA vaccines are also in progress. Furthermore, other trials are being conducted in specific subpopulations, such as in children under 16 years old and pregnant women. It is anticipated that by the end of 2021 there will be more clarity on the safety and efficacy of a full range of vaccines, and their use in children and pregnant women.

Two large multinational trials in 90,000 participants are underway to determine safety, efficacy and immunogenicity of the Johnson&Johnson/Janssen Ad26.COV2.S adenovirus viral vector vaccine. A single-dose regimen is being used in one of these trials, and success would significantly improve immunization coverage. The manufacturer expects to have sufficient data to apply to the UK Medicines Agency for emergency use authorization "within weeks". The vaccine could be stored in the refrigerator for up to three months.

However, to date, the most complete data is limited to the BioNTech/Pfizer and Moderna mRNA vaccines and the Oxford/Astra Zeneca (ChAdOx1 nCov-19) adenovirus vaccine. The available data for these three vaccines seem to suggest that they would be safe and efficacious in the population of Trinidad and Tobago. However, both the BioNTech/Pfizer, Moderna mRNA vaccines have stringent cold storage requirements, and it would be prudent to look more closely at the Oxford/Astra Zeneca (ChAdOx1 nCov-19) and other vaccines without these storage requirements. The Novavax protein subunit vaccine, which is expected to have complete data by the latter part of 2021, should also be considered as a possible alternative.

We must continue to monitor the safety and vaccine efficacy data coming out of global mass vaccination programs, especially those with ethnic subgroups that reflect our population, as well as in our own population as soon as local roll-out commences.

It is noteworthy that, currently, the duration of protection of all approved vaccines remains unknown.

A key strategy to build confidence in the population is the careful selection of the index recipient who would become the "face" of the vaccination campaign. We recommend someone of high integrity and trustworthiness who would be able to enthuse others to do likewise.

It would be critical that mechanisms be instituted for post-vaccination surveillance that would build trust and ensure public safety.

1. Background and Summary Statements

In December 2019, a new coronavirus emerged in Wuhan, China as a pneumonia of unknown origin. The coronavirus disease (COVID-19), caused by SARS-CoV-2, was officially named by the World Health Organization (WHO) and by March 11 it was declared a pandemic. According to the Johns Hopkins Coronavirus Resource Center there are over 82 million confirmed cases, and almost 1.8 million deaths globally as of December 29, 2020. In Trinidad and Tobago, with its first reported case on March 12, there has been a significant surge in recent months with over 7,000 confirmed cases and 126 deaths. It is important to note that the actual numbers of cases may be much higher than reported, as asymptomatic people or those with mild symptoms may not be tested. These individuals unwittingly pose a risk of infection to others, including more vulnerable individuals.

Enforcement of public health measures, such as mask wearing, physical distancing and hand washing, have helped to stymie the spread of infection. At the onset of the pandemic many governments imposed full shutdowns, closed borders, and restricted movement of people except those in essential services. These extreme measures have crippled many economies, and more recently several countries have imposed further partial shutdowns or more social restrictions to mitigate against the emergence of a "second wave" while trying to manage disastrous economic outcomes.

The determined search to repurpose drugs for prophylactic and therapeutic use in the fight against COVID-19 continues. However, most clinical studies have found that many of these drugs were no better than placebo to prevent or treat symptoms, and some of these drugs also pose serious risk of adverse reactions.

In parallel, the search for vaccines began using several approaches (or platforms) aimed at reducing the time to full development and commencement of clinical trials. The unprecedented success in bringing effective vaccines to the public in less than a year is now thought to be the way forward to some level of "normalcy" through mass immunization programs worldwide.

1.1 Vaccine Platforms and Innovative Approaches

Until recently, vaccine development focused on virus- or protein-based vaccines, which are now commonly used in routine immunization schedules. These include inactivated whole virus, live-attenuated, bacterial, protein sub-unit and protein conjugated vaccines, which usually take years in clinical development. Despite considerable use, vaccines developed using these approaches have numerous disadvantages, including the ability of live-attenuated strains to elicit vaccine-induced disease in immunocompromised individuals. Thus, researchers have developed new platforms to produce safe and efficacious vaccines, and these novel approaches have yielded effective COVID-19 vaccines at "warp-speed".

Viral vector vaccines, such as the University of Oxford/Astra Zeneca vaccine, are based on an approach that led to the development of commercially available Ebola vaccines. This approach was readily adapted to produce an effective vaccine against SARS-CoV-2. The viral vector platform uses a human virus such as an altered adenovirus, which acts as a shell to deliver genes for SARS-CoV-2 spike protein into host cells. Host cells use the spike protein genes to produce and secrete SARS-CoV-2 spike proteins which are then recognized as foreign by the host's immune system. Subsequently, a robust immune response is mounted against the SARS-CoV-2 spike protein. The altered adenovirus is unable to multiply or cause infection in the host. DNA- and RNA-based platforms use small segments of viral genome or products from the genome that code for viral antigens, particularly those that are important in helping viruses infect host cells. For example, the BioNTech and Moderna mRNA vaccines deliver RNA for the SARS-CoV-2 spike protein which host cells use to produce and secrete spike proteins, which are recognized by the host immune system to generate an immune response. The advantage of this platform is that it allows for very rapid development of vaccines.

1.2 Safety Issues

Immunization has played a huge role in reducing the incidence and prevalence of many deadly infectious diseases. However, rare occurrences of vaccine-induced severe adverse events have meant that global vaccination programs need to be constantly vigilant to reassure the public on vaccine safety in the face of growing anti-vaccination sentiments.

1.3 Public Perceptions

The rapid development of COVID-19 vaccines has caused a heightened public suspicion regarding safety, and spawned an array of conspiracy theories and misinformation on social media. Anti-vaxxers, those against vaccines, have perpetuated unproven links between vaccines, and/or additives, and a range of disorders including autism, autoimmune diseases, cancers and Alzheimer's disease.

Anti-vaccination myths and conspiracy theories regarding COVID-19 vaccines center around what some consider to be the lack of rigorous and stringent testing to ensure vaccine safety. The use of novel platforms, such as mRNA, has also led to conspiracy theories that this genetic material will be incorporated into human DNA and alter the genome. There have also been conspiracy theories surrounding the use of mass vaccination programs to facilitate implantation of microchips.

Some religious bodies, along with anti-vaxxers, continue to advocate that vaccines are not necessary since the body is well able to mount its own defense mechanisms against infections, including Covid-19.

These concerns must be addressed through public education strategies that provide clear and easy-to-understand messaging regarding safety and efficacy from robust clinical trials in diverse populations.

1.4 Public Education and Rollout of Vaccines

The development of a pro-vaccination strategy to guide public education and the rollout of the vaccination campaign/ programme is crucial to maximize vaccine uptake. This strategy must include, but is not limited to, audience targeting and dissemination; a marketing promotion strategy; media relations and outreach; and community engagement. A key strategy to inspire confidence in the population at large is the careful selection of the index recipient who would be the "face" of the immunization campaign in Trinidad and Tobago. We recommend someone of repute who would inspire their peers to do likewise. Research should be conducted to identify misinformation, misconceptions and conspiracy theories that are prevalent in the local setting. This is further explored in the chapter on beliefs and misconceptions about COVID-19 vaccines and strategies to improve vaccine uptake in the public health care system.

Summary Statements

- Over fifty (50) vaccines are listed by WHO as being in current clinical development, of which about twelve (12) are currently in Phase 3 trials.
- Two mRNA-based vaccines have received FDA Emergency Use Authorization- BioNTech/Pfizer (BNT162b2) and Moderna (mRNA-1273). The former has also been authorized for use by the MHRA in the UK.
- The Pfizer vaccine (BNT162b2) has been shown to have 95% efficacy in preventing COVID-19 infection. This vaccine requires storage at ultra-low temperatures of -70oC.
- The Moderna vaccine (mRNA 1273) has an overall vaccine efficacy of 94%. This vaccine does not require ultra-low refrigeration and once opened it could be stored in the refrigerator between 2oC to 8oC for up to one month.
- The University of Oxford/Astra Zeneca vaccine (ChAdOx1 nCoV-19) has shown vaccine efficacy of 62.1 or 90.0% depending on the regime used. This vaccine was approved for use in the UK and will be available in January 2021. Storage occurs from 2o C to 8oC and can be kept at that temperature for six months.
- The duration of protection of these vaccines is unknown as participants in these trials are still being monitored over the long term.
- The Sputnik V and EpiVacCorona vaccines are already approved in Russia for mass vaccination, but this follows small Phase I and II trials and little published clinical data to assess safety and efficacy.
- Several other promising vaccine candidates (CORONAVAC, Ad26.CoV2.S and BBIBP-CORV) are currently in large, well-designed Phase 3 trials with interim results expected by mid-2021.
- Several small Phase 1 and 2 clinical trials have highlighted promising vaccine candidates with data showing robust immune responses and acceptable safety profiles.
- Current large clinical trials do not include children under 16 years of age. Until trials provide safety and efficacy data in children it would not be advisable to implement a vaccination drive in this subpopulation.

- High rates of vaccines reactogenicity with mild to moderate local and systemic reactions have been reported following the second dose of BioNTech/Pfizer and Moderna vaccines and may be similar in upcoming vaccines. Potential vaccinees will have to be educated about these reactions and appropriate treatments.
- Recent reports in the media have highlighted rare occurrences of anaphylactic reactions following immunization with the BioNTech/Pfizer mRNA vaccine. These are being investigated by FDA and CDC in the USA.
- Maintenance of a “cold-chain” will be critical for delivery of some vaccines, such as the BioNTech/Pfizer vaccine which requires refrigeration at –70oC.
- Well-conceived public health programmes, including community engagement, are needed to counteract significant misconceptions among members of the public and improve vaccination uptake.
- Many developed countries have purchased several different types of vaccines for their populations. This approach has the advantage of giving members of the public a choice of what they receive and providing a range of vaccines that may be best suited for different subpopulations.

2. Approved/Authorised Vaccines

The World Health Organization listed six mRNA COVID-19 vaccines that were undergoing clinical trials. Two, the BioNTech/Pfizer (BNT 162b2) and Moderna-1273, have received FDA Emergency Use Authorization and are currently in use in the USA and UK. The other four candidates are in Phase I or II clinical trials. The focus of this report on mRNA vaccines is on the BioNTech/Pfizer and Moderna vaccines. These vaccines have stringent low temperature delivery and storage requirements, with the BioNTech vaccine requiring an ultra-low temperature of –70oC.

I. VACCINE name: BNT162b2

Manufacturers:
BioNTech/Pfizer

Vaccine platform:
a lipid nanoparticle-formulated, nucleoside-modified RNA vaccine encoding the SARS-CoV-2 full length spike protein, modified by 2 proline mutations to lock it in the prefusion conformation. The vaccine is stored at -70oC.
Availability: Available for emergency use in UK and USA.

Brief summary:
A multi-national, placebo-controlled, observer-blinded, pivot efficacy trial (Phase 3 trial). Approx. 44,000 participants randomly assigned in 1:1 ratio to receive vaccine or saline. Two doses of vaccine (30µg, 0.3ml) administered 21 days apart. Patients observed for 30 minutes post vaccination.

Multinational study:
USA (77%), Argentina (15%), Brazil (6%), South Africa (2%).

Overview of Study population:
Subgroups included diverse ethnicities; however, whites made up 83%; [age range 19-89, median age-52 years]; age group 16-55 (58 %); male: female (51%:49%); BMI ≥ 30 (35%).

Inclusion Criteria:
Safety population: 16 years and older [median follow up of 2 months in 37,706 persons, & reactogenicity subset, 8183 persons]; Healthy or had stable medical conditions including HIV, Hep B and Hep C.

Exclusion Criteria:
Medical history of COVID-19; treatment with immunosuppressive therapy; diagnosis with an immunocompromising condition.

Outcomes measurements:

Efficacy of the vaccine against laboratory-confirmed COVID-19 and safety:

- Efficacy of vaccines against confirmed COVID-19, seven or more days after the 2nd dose in participants without evidence of infection [36,523 persons evaluated],
- Efficacy in participant with and without prior evidence of infection [40,137 evaluated, suggests 3614 had prior infection] and
- Efficacy against severe COVID-19 infection.

Safety:

- Local or systemic adverse events and use of antipyretics or pain medication within 7 days after receipt of each dose of vaccine or placebo up to one month after the second dose and
- Unsolicited adverse events through 6 months after the second dose.

Adverse events data up to 14 weeks after the second dose were included and safety monitoring will continue for 2 years after administration of second dose.

Outcomes:

Efficacy:

- Eight cases in vaccinated group versus placebo group 162 at least 7 days after the 2nd vaccination (efficacy of 95% [90.3-97.6]).
- Similar efficacy for subgroups; 2178 participants of African and Mixed ethnicity with one case in vaccinated group versus 16 cases in placebo this sub-group.

Safety:

- Ten cases of severe COVID-19 with onset after the 1st dose; nine in placebo group versus one in vaccinated group.
- Safety over median 2 months of follow-up was “similar to other viral vaccines”:
  - » More systemic symptoms after 2nd dose but no difference in local symptoms following 1st and 2nd doses.
  - » Systemic symptoms after 2nd dose were more in younger age group, 16-55 compared with >55 group.
  - » Main local event- pain at injection site >> redness & swelling.
  - » Systemic symptoms- fatigue (59%) and headache (52%). Severe systemic events reported in <2% of vaccine recipients after either dose, though severe fatigue (3.8%) and severe headache (2%) after second dose.
- Overall, more adverse events in vaccinated group than placebo controls (27% vs 12%):
  - » Lymphadenopathy reported in 64 vaccinees and 6 placebo recipients
  - » 4 related serious AE (shoulder injury related to vaccine administration, right axillary lymphadenopathy, paroxysmal ventricular arrhythmia, right leg paresthesia)
  - » No deaths were considered by investigators to be related to vaccine or placebo

Overall quality of evidence:

Level II/High Grade/Low risk of bias

SUMMARY STATEMENT

This Phase 3 study showed high vaccine efficacy (95%) with safety over two months of follow-up "similar to other viral vaccines".

Persons ethnically similar to some in Trinidad and Tobago constituted about 10% of vaccinees, though they seemed to have been protected by the vaccine, there were no detailed breakdown of AE by ethnicity or gender, or by prior COVID-19 infection. Although Asians were included it is uncertain were South Asians (East Indians) which would represent similar ethnicity in T & T.

There was no information on what was meant by immunocompromised persons who were excluded from the study, while HIV infected individuals were included? There was no information on participants who were vaccinated but still got infected, especially the single severe case.

A major disadvantage to this vaccine is that it must be stored at ultra-low temperatures which could be a challenge for resource limited countries.

II. VACCINE name: mRNA 1273

Manufacturer:
Moderna

Vaccine platform:
The vaccine is based on the pre-fusion stabilized SARS-CoV-2 spike glycoprotein (S) antigen encoded by mRNA and formulated in a lipid nanoparticle (LNP). The vaccine (mRNA-1273) is a 2-dose series of 100-µg intramuscular injections given 1 month apart.

The vaccine is provided as a frozen suspension [stored between -25º to -15ºC] multi-dose vial containing 10 doses (0.5 mL each) which is thawed prior to administration. Vials can be stored refrigerated between 2° to 8°C for up to 30 days prior to first use. Unopened vials may be stored between 8° to 25°C (46° to 77°F) for up to 12 hours. After the first dose has been withdrawn, the vial should be held between 2° to 25°C (36° to 77°F) and discarded after 6 hours.

Availability:
Available for emergency use in the US.

Brief summary:
This study was conducted at 99 sites in the US. Participants (N=30,351) randomized 1:1 to receive intramuscular injections of either 100 µg of mRNA-1273 vaccine (n=15,181) or placebo (n=15,170) 28 days apart. Expected duration: 25 months.

Study participants:
Stratified by age and health risk into three groups:

- 18 to <65 years of age and not at risk for progression to severe COVID-19,
- 18 to <65 years of age and at risk for progression to severe COVID-19, and
- ≥65 years of age, with the latter two groups consisting of 41.4% of the study population.

Participants were considered at risk for progression to severe COVID-19 if they had underlying comorbidities including diabetes, chronic lung disease, severe obesity, significant cardiovascular disease, liver disease, or infection with HIV.

The study included 24,907 (82.1%) participants considered at occupational risk for acquiring SARS-CoV-2 infection, of whom 7,613 (25.1%) were healthcare workers.

Outcome measurements:

Efficacy:
Primary efficacy endpoint was efficacy to prevent COVID-19 infection at least 14 days after 2nd dose in participants with negative SARS-CoV-2 status at baseline.

Secondary endpoints based on the Per-Protocol Set included the vaccine efficacy to prevent the following:
Severe COVID-19.

- COVID-19 based on a less restrictive definition of disease (see below*) occurring at least 14 days after the 2nd dose of vaccine.
- COVID-19 occurring at least 14 days after the 2nd dose of vaccine in participants with or without prior Covid-19 infection.
- Death due to COVID-19.
- COVID-19 occurring at least 14 days after the 1st dose of vaccine (including cases that occurred after the 2nd dose).

Safety assessments:

- Solicited local and systemic adverse reactions (AR) that occurred during the 7 days following each dose (i.e., the day of vaccination and 6 subsequent days). Solicited ARs were recorded daily using eDiaries.
- Unsolicited AEs observed or reported during the 28 days following each dose (i.e., the day of vaccination and 27 subsequent days). Unsolicited AEs are those not included in the protocol-defined solicited AR.
- AEs leading to discontinuation from vaccination and/or study participation from Day 1 through Day 759 or withdrawal from the study.
- Medically Attended Adverse Events (MAAE) from Day 1 through Day 759 or withdrawal from the study.
- Serious Adverse Events (SAEs) from Day 1 through Day 759 or withdrawal from the study.
- Abnormal vital sign measurements.
- Physical examination findings.
- Pregnancy and accompanying outcomes.

Outcomes:

Efficacy:
Vaccine efficacy (VE) starting 14 days after 2nd dose was 94.1% (95% CI 89.3%, 96.8%), consistent with results from interim analysis.

VE in older participants (> 65 years) appears to be lower than in younger adults (18 to <65 years) [86.4% versus 95.6%] and lower than observed in the interim analysis (100% based on 15 cases).

Generally, VE among the subgroups was similar to VE seen in the overall study population. Small participant numbers and cases in some subgroups, such as those over 75 years of age and certain racial groups, limit interpretation of individual VE results.

Only 2.2% of participants had evidence of prior infection at enrollment, with only one COVID-19 case starting 14 days after dose 2 reported from this subgroup, which was in a participant in the placebo group. There is insufficient data to conclude on the efficacy of the vaccine in previously infected individuals.

Safety:
Adverse events (AE) were reported at a higher proportion in vaccinated versus placebo recipients; the imbalance driven by reactogenicity (solicited AEs) reported in the 7 days following each dose. The proportions of participants with SAEs, death, and withdrawals due to AEs were balanced across treatment groups.

Local AEs:
Solicited local AE were reported by most vaccine recipients at higher rates than placebo recipients. The proportions of vaccinees reporting any local AR were 84.2% and 88.8% after dose 1 and dose 2 versus 19.8% and 18.8% after dose 1 and dose 2 in placebo recipients, respectively. The proportions reporting at least one grade 3 local AR were 3.5% and 7.0% after dose 1 and dose 2, respectively in vaccine recipients and 0.5% after any dose in placebo recipients. The main symptom was pain lasting 2-3 days. Axillary lymphadenopathy in the vaccinated arm was the second most frequently reported local AE.

Systemic AEs:
Solicited systemic AE were reported for most vaccine recipients at higher rates than for placebo recipients. Vaccine recipients had higher rates of systemic reactions after the 2nd dose than the 1st dose. The proportions of vaccine and placebo participants reporting systemic AR were as follows: reporting any grade was 54.9% vs 42.2% after dose 1 and 79.3% vs 36.5% after dose 2 and reporting Grade 3 was 2.9% vs. 2.0% after dose 1 and 15.7% vs.2.0% after dose 2, respectively. The most frequently reported systemic AR was fatigue, followed by headache, myalgia, arthralgia, and chills.

Additional AE:
There were no anaphylactic or severe hypersensitivity reactions with close temporal relation to the vaccine. Throughout the safety follow-up period to date, there were three reports of facial paralysis (Bell's palsy) in the vaccine group and one in the placebo group. Currently available information is insufficient to determine a causal relationship with the vaccine.

A total of 30 severe COVID-19 cases starting 14 days after 2nd dose and all were given placebo.
Overall quality of evidence: Level II/High Grade/Low risk of bias

SUMMARY STATEMENT

This Phase 3 trial provided evidence of vaccine efficacy (94.1%) and safety of Moderna mRNA 1273. The higher rates of local and systemic adverse events in the vaccine versus placebo could probably be due to the general reactogenicity of vaccines. An advantage of the vaccine for resource limited countries is that it could be stored refrigerated temperatures for up to 30 days after vials are opened.

*Less restricted definition of COVID-19 infection - a positive NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) for SARS-CoV-2 by RT-PCR and one of the following systemic symptoms including fever (temperature ≥38°C), chills, cough, shortness of breath or difficulty breathing, fatigue, muscle aches or body aches, headache, new loss of taste or smell, sore throat, nasal congestion or rhinorrhea, nausea or vomiting, or diarrhea.

III. VACCINE name: ChAdOx1 nCoV-19

Manufacturer:
Oxford University/Astra Zeneca

Vaccine platform:
A replication-deficient chimpanzee adenoviral vector, ChAdOx1, containing the SARS-CoV-2 structural surface glycoprotein antigen (Spike protein) gene. The simian adenovirus was utilized to overcome any pre-existing immunity participants may have to human adenoviruses thus reducing their immunogenicity.
Availability: APPROVED and available in the UK from 4th January 2021. Phase 3 studies continuing.

Brief summary:
These studies aim to determine the efficacy, immunogenicity and safety of ChAdOx1 nCoV-19 in different age groups, health states, genders, and ethnicities. Analysis provides data on four ongoing blinded, randomized, controlled trials conducted in three countries.

COV001 – Phase 1 / 2 – UK

Trial Registration #: NCT04324606
Ongoing, single-blind, 1077 participants, 18 – 55 years., randomly assigned to receive ChAdOx1 nCoV-19 at a dose of 5 × 1010 viral particles (standard dose), or meningococcal group A, C, W and Y conjugate vaccine (MenACWY) as control. MenACWY consists of polysaccharides from serogroups A, C, W and Y (from meningococcal capsule) conjugated to a tetanus or diphtheria toxoid carrier protein. MenACWY was used as a comparator vaccine rather than a saline placebo to maintain masking of participants who had local or systemic reactions. A subgroup of ten participants was given two doses 28 days apart. Due to the evaluation of early immunogenicity cohorts and the result of robust booster responses, the protocol was modified to a two-dose regime, with the booster given at the earliest time.

COV002 – Phase 2 / 3 - UK

Trial Registration #: NCT04400838, NCT04400838
Ongoing single-blind, 18 years and older. Two dosage groups: participants who received low dose – 2.2 x 1010 viral particles as 1st dose, boosted with standard dose (LD/SD); 2nd group participants received two standard doses (SD/SD).

COV003 – Phase 3 – Brazil

Trial Registration #: NCT04536051
Ongoing single blind, 18 years and older, participants had stable pre-existing health conditions. All were offered two doses of vaccine at 3.5 - 6.5 x 1010 viral particles given up to 12 weeks apart (target was 4 weeks).

COV005 – Phase 1/2 – South Africa

Trial Registration #: NCT04444674, NCT04444674
Ongoing double-blind, healthy adults, 18 – 65 years. Two doses of the vaccine at 3.5 - 6.5 x 1010 viral particles, administered 4 weeks apart.

Table 1. Baseline characteristics of participants included in the primary efficacy population, by study and dosing strategy.

		COV002 (UK; LD/SD; N=2741)		COV002 (UK; SD/SD; N=4807)		COV003 (Brazil; all SD/SD; N=4088)	
		ChAdOx1 nCoV-19 (n=1367)	MenACWY (n=1374)	ChAdOx1 nCoV-19 (n=2377)	MenACWY (n=2430)	ChAdOx1 nCoV-19 (n=2063)	MenACWY + saline (n=2025)
Age, years	18–55	1367 (100·0%)	1374 (100·0%)	1879 (79·0%)	1922 (79·1%)	1843 (89·3%)	1833 (90·5%)
	56–69	0	0	285 (12·0%)	293 (12·1%)	209 (10·1%)	187 (9·2%)
	≥70	0	0	213 (9·0%)	215 (8·8%)	11 (0·5%)	5 (0·2%)
Sex	Female	886 (64·8%)	927 (67·5%)	1378 (58·0%)	1437 (59·1%)	1261 (61·1%)	1156 (57·1%)
	Male	481 (35·2%)	447 (32·5%)	999 (42·0%)	993 (40·9%)	802 (38·9%)	869 (42·9%)
BMI, kg/m^2		25·2 (22·8–28·7)	25·3 (22·7–28·8)	25·4 (22·9–28·7)	25·5 (22·9–29·1)	25·6 (22·8–29·1)	25·6 (23·1–29·0)
Ethnicity	White	1257 (92·0%)	1278 (93·0%)	2153 (90·6%)	2214 (91·1%)	1357 (65·8%)	1366 (67·5%)
	Black	6 (0·4%)	2 (0·1%)	17 (0·7%)	14 (0·6%)	230 (11·1%)	210 (10·4%)
	Asian	76 (5·6%)	59 (4·3%)	137 (5·8%)	138 (5·7%)	54 (2·6%)	53 (2·6%)
	Mixed	19 (1·4%)	22 (1·6%)	48 (2·0%)	42 (1·7%)	410 (19·9%)	386 (19·1%)
	Other	9 (0·7%)	13 (0·9%)	22 (0·9%)	22 (0·9%)	12 (0·6%)	10 (0·5%)
Health and social care setting workers		1236 (90·4%)	1253 (91·2%)	1441 (60·6%)	1513 (62·3%)	1833 (88·9%)	1775 (87·7%)

		COV002 (UK; LD/SD; N=2741)		COV002 (UK; SD/SD; N=4807)		COV003 (Brazil; all SD/SD; N=4088)	
		ChAdOx1 nCoV-19 (n=1367)	MenACWY (n=1374)	ChAdOx1 nCoV-19 (n=2377)	MenACWY (n=2430)	ChAdOx1 nCoV-19 (n=2063)	MenACWY + saline (n=2025)
Comorbidities	CVD	104 (7·6%)	92 (6·7%)	264 (11·1%)	266 (10·9%)	271 (13·1%)	244 (12·0%)
	Respiratory disease	158 (11·6%)	176 (12·8%)	285 (12·0%)	316 (13·0%)	215 (10·4%)	210 (10·4%)
	Diabetes	18 (1·3%)	15 (1·1%)	58 (2·4%)	60 (2·5%)	59 (2·9%)	60 (3·0%)

Outcome measurements:

- Efficacy of ChAdOx1 nCoV-19 vaccine against COVID-19 in adults (number of virologically confirmed symptomatic cases of COVID-19). Efficacy was calculated as the proportionate reduction in the event rate between vaccinated and non-vaccinated individuals.
- Safety of ChAdOx1 nCoV-19 vaccine in adults (occurrence of serious adverse events, SAEs).
- Immunogenicity.

Outcomes:

- Combined UK and Brazil trials gave vaccine efficacy of 70.4% (South Africa not included).
- For UK arm, vaccine efficacy differed between LD/SD and SD/SD with 90% versus 60.3%. For the Brazil arm (SD/SD) vaccine efficacy was 64.2%.
- Since the timing of priming and booster vaccine administration varied among studies, efficacy among the different timings was also analyzed.
- COV002 (UK): Vaccine efficacy was 90% in the LD/SD group whilst it was 65.6% in the SD/SD group when there was an >8 weeks interval between vaccine doses.
- COV003 (Brazil): <6 weeks interval = 53.4% while ≥ 6 weeks' interval = 65.4%
- Older participants were not assessed for efficacy but would be included in future analysis as more cases accrue.
- In COV002, the ChAdOx1 nCoV-19 vaccine induced a specific antibody response to the Spike protein and the receptor binding domain (RBD) across all age groups after one dose. Boost vaccination had an increased effect on antibody titres unrelated to dose regimen or age group.
- Regarding immunogenicity, T cell responses against SARS-CoV-2 spike protein were measured via an IFN-γ assay. The response peaked on day 14 and remained consistent up to day 56 post vaccination, regardless of dosage or age group.

Safety:

Serious adverse effects occurred in 168 participants, 79 in vaccine group and 89 in placebo/saline group. Three cases of transverse myelitis, one idiopathic, short segment, spinal cord demyelination and other two deemed unrelated to the vaccination trials.

Lower dose was less reactogenic than standard dose across all age groups, while fewer AEs were reported after booster vaccine than after primer vaccine for those who received two doses.

Overall quality of evidence: Level II/High Grade/Low risk of bias.

These trials were blinded, randomized and controlled, sufficiently powered to detect differences in infection rates between vaccinated and non-vaccinated groups.

Duration of protection:
Not known, studies are ongoing.

Notes:
1. Analysis did not include South African participants; this would be of interest, especially in our local setting with similar ethic groups.
2. Desegregating results in older persons, those with comorbidities and allergies would be of particular interest as these individuals are considered at high-risk.
3. Long-term follow-up is needed to provide data on duration of protection of the ChAdOx1 nCoV-19 vaccine.

SUMMARY STATEMENT

Interim results in the ChAdOx1 nCoV-19 trial have provided initial data on safety and efficacy for the vaccine which prevents infection by initiating humoral and cell-mediated immune responses.

UPDATE: 30/12/2020 - This vaccine has been approved for use in the United Kingdom with two full/standard doses being given, 2nd dose given at four to twelve weeks post first inoculation. Though preliminary studies showed greater efficacy of the vaccine when given at a low dosage followed be a standard dose, the number of participants were smaller and none were older than 55 years.

Advantages – The Oxford vaccine can be stored at 2oC – 8oC for up to six months and costs less than Pfizer or Moderna vaccines.

IV. VACCINE name: Sputnik v/Gam-Covid-Vac (frozen and lyophilized formulations)

Manufacturer:
Gamaleya Research Institute/Russian Direct Investment Fund (RDIF) collaborating with Acellena Contract Drug Research and Development.

Vaccine platform:
non-replicating recombinant human adenovirus vectors, both carrying the gene for the SARS-CoV-2 full length glycoprotein S: adenovirus type 26 (rAd26-S) and adenovirus type 5 (rAd5-S) vectors.

Trial Registration #: NCT04436471, NCT04437875, NCT04436471, NCT04437875, NCT04587219, NCT04530396

Availability:
Distribution begins January 2021. Countries have already procured vaccines with delivery started in March 2021. Although the manufacturers have applied, they are yet to receive WHO Emergency Use Listing/Prequalifiaction (WHO EUL/PQ) for the vaccine.

Brief summary:
Phase 1/2 studies conducted. Phase III studies in progress.

- Phase 1 - One dose (im) of either rAd5-S or rAd26-S in either frozen or lyophilized form. Immune assessment on day 0 and day 20 post-injection
- Phase 2 – Vaccination (im) of rAd26-S on day 0 followed by rAd5-S on day 21. Immune assessment on days 0, 28 and 42 post-injection.

Table 2. Baseline characteristics of participants included in the primary efficacy population, by study and dosing strategy.

		Gam-COVID-Vac			Gam-COVID-Vac-Lyo		
		rAd26-S (n=9)	rAd5-S (n=9)	rAd26-S + rAd5-S (n=20)	rAd26-S (n=9)	rAd5-S (n=9)	rAd26-S + rAd5-S (n=20)
Sex	Male	9 (100%)	9 (100%)	14 (70%)	5 (56%)	2 (22%)	14 (70%)
	Female	0	0	6 (30%)	4 (44%)	7 (78%)	6 (30%)
Height, m		1·8 (0·1)	1·8 (0·1)	1·7 (0·1)	1·7 (0·1)	1·7 (0·1)	1·8 (0·1)
Bodyweight, kg		80·6 (6·0)	83·4 (13·8)	74·6 (12·5)	72·1 (13·1)	65·8 (9·4)	72·0 (12·6)
Age, years		27·8 (5·1)	25·3 (6·1)	26·4 (4·4)	31·4 (8·2)	27·0 (7·7)	26·7 (5·8)
Ethnicity	White	9 (100%)	9 (100%)	20 (100%)	8 (89%)	9 (100%)	19 (95%)
	Asian	0	0	0	1 (11%)	0	1 (5%)
SARS-CoV-2 IgM and IgG -ve		9 (100%)	9 (100%)	20 (100%)	9 (100%)	9 (100%)	20 (100%)

Outcomes measurements:
Immunogenicity - change from baseline to day 42 in antigen-specific antibody levels, measured by ELISA.
Safety - number of participants with AEs from day 0 to day 28 after vaccination (Phase 1); from day 0 to day 42 after vaccination (Phase 2).

Outcomes:

Immunogenicity
SARS-CoV-2 RBD-specific IgGs were detected in both formulations in Phase 1 trial; increased titres in Phase 2, where two doses given, at day 42. Only for Phase 2 trial was data was collected at day 42. Neutralising antibodies were also increased in participants who received both rAds in comparison to those who only receive one. CD4+ and CD8+ proliferation and IFN-γ production in Phase 1 trial, with increased numbers in Phase 2 trial. The presence of anti-vector immune cells did not affect titre of RBD-specific antibodies.

Safety
Most systemic AEs included pain at injection site, hyperthermia, headache, muscle and joint pain, asthenia. These effects were more prevalent in those given frozen vaccine as opposed to lyophilized formulation.

Duration of protection:
Unknown

Overall quality of evidence: Level III/Low Grade/High risk of bias

These Phase I trials were non-randomized, non-controlled, including 78 healthy white males in the military and under 30 years old. Neither of these trials had extended times to monitor the participants' responses before the vaccine was being used. A phase 3 trial is needed to have a robust evaluation of the vaccine's efficacy and adverse effect profile.

SUMMARY STATEMENT

The Sputnik V is a combination of rAd26-S and rAd5-S adenovirus vaccines with an induction of both humoral and cell-mediated responses. The limited data suggests that it is more efficacious as a combination treatment versus a single dose of either vector vaccine. The lyophilized form may be beneficial in communities that lack ultra-low refrigeration capacity.

V. Vaccine name: EpiVacCorona

Manufacturer:
Federal Budgetary Research Institution State Research Center of Virology and Biotechnology, Vektor – Russia

Availability:
Approved for mass vaccination in Russia starting from 01st January 2021. Phase I/II started on 27th July 2020, estimated completion 4th October 2020. [NCT04527575]. Phase 3 trials started to include 3000 adults over 18 years and 150 over 60 years.

Vaccine platform:
Synthetic peptide antigens of SARS-CoV-2 proteins, conjugated to a carrier protein and adsorbed on an aluminum-containing adjuvant - provokes an immune reaction against COVID-19 and promotes the further development of immunity.

Brief Summary:
Phase 1/2, single-blind, placebo-controlled, randomized study. In 100 healthy male and female volunteers aged 18 to 60 years old to determine the safety, reactogenicity and immunogenicity parameters of the EpiVacCorona vaccine (0.5 mL) given as two doses, 21 days apart.

Outcome measurements
- Evaluate the safety of the EpiVacCorona vaccine when administered twice im.
- Evaluate the reactogenicity of the EpiVacCorona vaccine when administered twice im.
- Identify the development of adverse reactions to vaccine administration.
- Humoral and cellular immune responses following two doses of EpiVacCorona vaccine.

Three treatment groups
- Group 1: 14 volunteers vaccinated with EpiVacCorona vaccine twice 21 days apart, intramuscularly.
- Group 2: 43 volunteers vaccinated with EpiVacCorona vaccine twice 21 days apart.
- Group 3: 43 volunteers given placebo (sodium chloride, 0.9%) im twice 21 days apart.

Safety:
Not known. No results published in scientific literature.

Overall Quality Of Evidence:
Not known. Not results published in scientific literature.

Status:
Completed. No results published in scientific literature.

VI. VACCINE name: BBIBP-CorV - PHASE I/II TRIAL

Manufacturer:
Beijing Institute of Biological Products/Sinopharm.

Vaccine platform:
Three isolated SARS-CoV-2 strains [19nCoV-CDC-Tan-HB02 (HB02), 19nCoV-CDC-Tan-Strain03 (CQ01), and 19nCoV-CDC-Tan-Strain04 (QD01)] were used to develop preclinical in vitro neutralization and challenge models for an inactivated SARS-CoV-2 vaccine candidate. The three strains were Vero cells, but not other cell lines, were infected via the throat swabs of patients to prevent possible mutations during viral culture and isolation.

HB02 strain showed the most optimal replication and generated highest virus yields in Vero cells among three viral strains and was therefore used for the development of the inactivated SARS-CoV-2 vaccine (BBIBP-CorV).

To inactivate virus production, β-propionolactone was thoroughly mixed with the harvested viral solution at a ratio of 1:4,000 at 2-8°C. The inactivation of three batches of virus eliminated viral infectivity, validating the good stability, and repeatability of the inactivation process. Western blot analysis showed that the vaccine stock contained viral structural proteins (protective antigens). A negatively stained electron microscopy image visualized oval viral particles with spikes with the diameters of approximately 100nm.

Availability:
Not available.

Brief summary:
A randomized, double-blind, placebo-controlled, phase 1/2 trial conducted in Shangqiu City Liangyuan District Center for Disease Control and Prevention in Henan Province, China.

Phase 1:
1,192 participants received either vaccine or placebo in a two-dose schedule: 2 dose schedule of 2 μg, 4 μg, 8 μg on Days 0 and 28.

Phase 2:
448 participants received single-dose schedule (8 μg) or a 2-dose schedule (4 μg) of on Days 0 and 14, Days 0 and 21, or Days 0 and 28.

Inclusion:
Healthy people aged 18–80 years, negative for serum-specific IgM/IgG antibodies against SARS-CoV-2 at baseline.

Exclusion:
History of travelling to Hubei Province (China), regions outside of China, or regions with reported COVID-19 cases from December 2019. History of infection with SARS-CoV; fever, cough, runny nose, sore throat, diarrhoea, dyspnoea, or tachypnoea in the 14 days before vaccination. Abnormalities in laboratory tests; pregnancy or lactation; a history of seizures or mental illness; and being unable to comply with the study schedule.

Outcome measurements

- ***Humoral immunogenicity***: Measured using an infectious SARS-CoV-2 neutralising assay and expressed as neutralising antibody geometric mean titre (GMT).
- ***Safety***: Adverse reactions within 7 days after the 1st and 2nd vaccinations.
- ***Secondary safety endpoints***: Abnormal changes in laboratory measures at day 4 post inoculations, and adverse events within 28 days after the first and the second vaccinations.

Outcomes

Phase 1:
Humoral immunogenicity - Neutralising antibody geometric mean titres, day 42: **18–59 years** - 2 µg: **87·7** [95% CI 64·9–118·6]; 4 µg: **211·2** [158·9–280·6]; 8 µg: **228·7** [186·1–281·1] ; **60 years and older** - 2 µg: **80·7** [65·4–99·6]; 4 µg: **131·5** [108·2–159·7]; 8 µg: **170·87** [133·0–219·5].

Placebo group (**2·0**) [2·0–2·0]).

Safety - Adverse reactions (first 7 days) - 42/144 (29%). The most common systematic adverse reaction was fever - one [4%] in the 2 µg group, one [4%] in the 4 µg group, and two [8%] in the 8 µg group. No serious adverse event was reported within 28 days' post vaccination.

Phase 2:
Humoral immunogenicity - The vaccine-elicited neutralising antibody titres for the 4 µg group on day 28: Days 0 and 14 (**169·5**, 95% CI 132·2–217·1); Days 0 and 21 (**282·7**, 221·2–361·4); Days 0 and 28 (**218·0**, 181·8–261·3); 8 µg Day 0 schedule (**14·7**, 11·6–18·8).

Safety - The most common systematic adverse reaction was fever. One placebo recipient in the 4 µg days 0 and 21 group reported grade 3 fever but was self-limited and recovered. All other adverse reactions were mild or moderate in severity.

Overall quality of evidence: Level III/High Grade/Low risk of bias.

These trials were randomized, double-blinded and placebo-controlled.

SUMMARY STATEMENT:

The phase 2 trial has demonstrated low adverse effect profile and a high neutralising antibody response in the group treated with 4 µg vaccines on days 0 and 21. Larger Phase 3 studies are needed to determine vaccine efficacy and long-term safety.

STATUS: Phase 1/2 trials completed.

3. Beliefs and Misconceptions about COVID-19 Vaccines and Strategies to Improve Vaccine Uptake in the Public Health Care System

3.1 Background

On 23rd September 2020, the Ministry of Health, Trinidad and Tobago (T&T) signed a commitment letter to join the COVAX Vaccine Facility, one of three pillars of the Access to COVID-19 Tools (ACT) Accelerator, launched in April by the World Health Organization (WHO), the European Commission and France, in response to this pandemic. Coordinated by Gavi, the Vaccine Alliance, the Coalition for Epidemic Preparedness Innovations (CEPI) and the WHO, the COVAX pillar aims to ensure that there is fair and equitable access to COVID-19 vaccines. COVAX will achieve this by acting as a platform that will support the research, development, and manufacturing of a wide range of COVID-19 vaccine candidates and negotiate their pricing. All participating countries, regardless of income levels, will have equal access to these vaccines once they are developed.

As the Ministry of Health prepares to launch its COVID-19 vaccination campaign/programme in 2021, consideration must be given to the misinformation and disinformation campaigns, as well as a myriad of conspiracy theories related to the COVID-19 pandemic, and by extension the development and roll-out of vaccines needed to end the acute phase of the pandemic. To maximise vaccine uptake, WHO recommends that countries develop a COVID-19 pro-vaccination strategy in advance of vaccine availability, to build a consensus about the order in which groups of the population will get access to the vaccine; to reduce any fear and concerns that exist in relation to vaccination; and to create demand for vaccines.

This document presents the findings of a rapid review of the literature/evidence on common beliefs and misconceptions about COVID-19 vaccines, as well as a summary of WHO key guidelines that should comprise a pro-vaccination strategy that can be implemented in the public health care system to facilitate vaccine uptake. This document does not provide a full review of the literature.

3.2 Method

A comprehensive search strategy was developed using the key words, databases, and search strings in Box 1. Anecdotal evidence was included in the key findings.

BOX 1: SUMMARY OF SEARCH STRATEGY	
Keywords (MeSH Terms): **belief**; view; assumption; opinion; knowledge; attitude; practice; culture; understand* **misconception**; misunderstand*; misinform* **vaccine**; vaccination; immunization OR immunisation; pharmacolog*; inoculation **public health**; health system; health care OR healthcare; agency **address**; educat*; manage; approach; inform*; response; intervention; delivery **COVID-19**; Coronavirus; SARS-CoV-2	**Databases:** Health Systems Evidence Health Evidence Cochrane PubMed
Search Terms 1: (belief OR view OR assumption OR opinion OR knowledge) AND (misconception OR misunderstand* OR misinform*) AND (vaccin* OR immunization OR immunisation OR pharmacolog* OR inoculation) AND (COVID-19 OR Coronavirus OR SARS-CoV-2) **Search Terms 2:** (belief OR attitude OR practice OR culture OR understand*) AND (misconception OR misunderstand* OR misinform*) AND (vaccin* OR immunization OR immunisation OR pharmacolog* OR inoculation) AND (COVID-19 OR Coronavirus OR SARS-CoV-2) **Search Terms 3:** (belief OR view OR assumption OR opinion OR **knowledge) AND (misconception OR misunderstand* OR misinform*) AND (vaccin* OR immunization OR immunisation OR pharmacolog* OR inoculation)** **Search Terms 4:** (belief OR attitude OR practice OR culture OR understand*) AND (misconception OR misunderstand* OR misinform*) AND (vaccin* OR immunization OR immunisation OR pharmacolog* OR inoculation) **Search Terms 5:** (public health OR health system OR health care OR healthcare OR agency) AND (address OR educat* OR manage OR approach OR inform*) AND (vaccin* OR immunization OR immunisation OR pharmacolog* OR inoculation) **Search Term 6** (public health OR health system OR health care OR healthcare OR agency) AND (address OR educat* OR manage OR approach OR inform*) AND (misconception OR misunderstand* OR misinform*) AND (vaccin* OR immunization OR immunisation OR pharmacolog* OR inoculation) AND (COVID-19 OR Coronavirus OR SARS-CoV-2)	

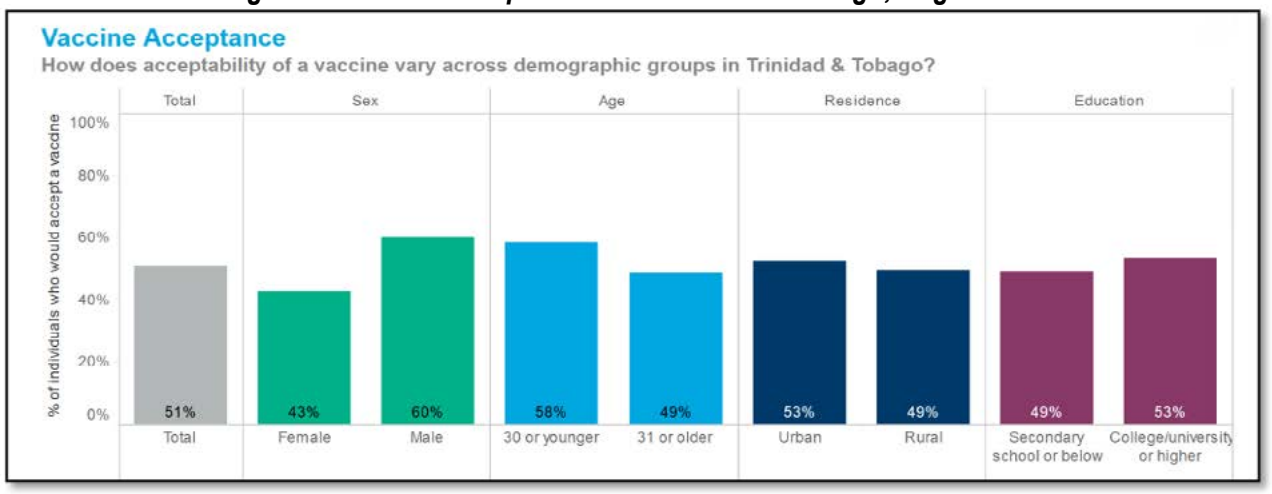
3.3 Summary Findings

3.3.1 Belief and Misconceptions

Vaccine hesitancy, defined as the delay in acceptance or refusal of vaccines despite the availability of vaccination services, is considered by WHO as one of the top ten threats to global health. Studies have demonstrated an association between willingness to get vaccinated and decreases with increased receptiveness to misinformation. Trust in vaccines/immunization programmes is a changing phenomenon driven by different reasons including, but not limited to, safety concerns, politics, religion, socioeconomic disparities, and misinformation. Identifying and debunking misconceptions, misinformation and conspiracy theories related to the COVID-19

vaccines are essential to maximize vaccine uptake, when they become available in 2021. A survey conducted by Johns Hopkins University that investigated the acceptance of a COVID-19 vaccine in 67 countries found that acceptability varied from 26%-85%. The report indicated that 51% of T&T responders would accept a vaccine in the future (see Figure 1).

Figure 1. Vaccine Acceptance in Trinidad and Tobago, August 2020



Source: https://ccp.jhu.edu/kap-covid/kap-covid-country-profiles-with-demographic-disaggregation/

At a conference on Vaccines and Immunity, hosted by The University of the West Indies, it was reported that a rapid survey of the Caribbean staff of the Expanded Programme on Immunization, found 74% were concerned about vaccine safety and content and 42% were concerned about vaccine efficacy and herd immunity. 79% agreed that there is a need for a vaccine introduction and communication plan.

3.3.2 The Anti-Vaccine Movement

The Anti-vaccine Movement, that is, organizations that believe that vaccines are very harmful, can be considered a major obstacle to vaccine uptake. Mistrust of government, and a set of "alternative facts" and incorrect views are held and propagated by the movement. In a study that examined COVID-19 related claims from a popular anti-vaccine broadcast in the United States of America (USA), the following six common themes were identified and matched to their anti-vaccine equivalents.

Table 1
Themes from The Highwire with anti-vaccine comparison.

Theme	Description	Anti-Vaccine Equivalent
1. "They" are lying to you	The government, "Big Pharma," and other entities are hiding the truth about COVID-19 cases and fatalities from the general public; suggestion that disease is more mild than reported.	The government, "Big Pharma," and other entities are hiding the truth about vaccine injuries and deaths from the general public.
2. Civil liberties	Government has no right to impose stay-at-home orders; quarantine is worse than the disease.	"My child, my choice;" argues that parents should be the sole arbiter of vaccine uptake and vaccine mandates should be removed.
3. Everyone is an expert	Belief that developing scientific expertise is not difficult nor need to be specialized.	Parents know their children best; parents are experts on children.
4. Science won't save us (nature is better)	Promotion of herd immunity for SARS-CoV-2 infections.	Promotion of "natural" infection in place of vaccination.
5. Skew the science	Cherry-pick experts who are outside of the mainstream to suggest particular areas of COVID-19 epidemiology are more controversial than they appear.	Cherry-pick experts who are outside of the mainstream to suggest vaccinations are more dangerous than mainstream science accepts.
6. "They" are out to harm you	The government and "Big Pharma" want to use COVID-19 to depopulate the globe and inject the population with tracking devices.	The government and "Big Pharma" want to use vaccines to depopulate the globe and inject the population with tracking devices.

3.3.3 Common Misconceptions and Conspiracy Theories

Below are some of the common misconceptions and conspiracy theories related to vaccines:

- **Myths carried over from previous vaccine regimes (Measles, Mumps, and Rubella (MMR), Polio, Diphtheria (DPT))**
  Myths carried over from existing vaccine regimes are being extended to the development and use of vaccines for the COVID-19 prevention. Some of these include the development of neurological disorders from the use of DTP and MMR and impotence and other complications from the use of oral polio vaccine.

- **Unsafe because it was rushed**
  The unprecedented speed with which the COVID-19 vaccines were developed and distributed for immunization programmes, has fuelled a lack of confidence.
  Vaccines pass through five stages of development and can take more than 10 years to fully develop. The fastest vaccine, which took four years to be produced, was developed for mumps.

- **Adjuvant ingredients unsafe**
  There is the belief that adjuvants, which boost or enhances immune response, in vaccines will be harmful. This is fuelled by the anti-vaxxers and a general lack of understanding of how adjuvants work to encourage the body to respond to vaccines more vigorously, making them more effective.

- **Religion/Ethnicity exploitation of some ethnic group**
  The exploitation of black and brown people for the advancement of medicine falls under the umbrella of medical racism. Ethnic minorities in the USA and the United Kingdom (UK) have been reported to be disproportionately affected by COVID-19. Historical examples include the ethical violations of withholding syphilis treatment from black men

under the Tuskegee Study in the USA, exposure of non-consenting predominantly black people to cancer radiation in a USA government study, perfecting surgical techniques on enslaved black women without consent, syphilis study on Latinos in Guatemala, etc. The belief and fear among people of colour is that they will be used as Guinea pigs for the true rollout of the vaccine. These fears extend from the USA to UK and Australia where people of colour also experience many barriers accessing and receiving healthcare.

Distrust among some religious groups, Muslims for example, is not necessarily based on religion principles, but more so on concerns for safety and poor communication of information. The objections to polio by religious and political fundamentalists in Nigeria, Pakistan and Afghanistan raised suspicion of a ploy to sterilize the Muslim populations through vaccination.

- **Continuation of routine mask wearing is not necessary**
  There is a misconception that the COVID-19 vaccine means you will not test positive for COVID-19 and there is no need for wearing a mask over nose and mouth. There is also the myth that because you have been exposed to COVID-19 or are recovered from COVID 19, you would not need to take the test again.

- **Population control**
  Mistrust of vaccines is also tied to belief and/or misinformation around plots to sterilise or infect populations to reduce population numbers. This was typically believed among non-Western countries, but this disinformation is also circulating among the Western countries with the prospect and release of a COVID-19 vaccine. The work of philanthropist Bill Gates in public health and his involvement in vaccine manufacturing and distribution to the developing world has also been tied to this misconception.

- **Induce DNA mutations**
  Social media has circulated claims that philanthropist Bill Gates plans to use vaccines to induce DNA mutation.

- **5G conspiracies and GPS tracking components (micro-chip)**
  Globally and locally, there is disinformation circulating on social media about the capability of 5G mobile phone signals to transmit signals to reduce the body's defense against COVID-19. In addition, there is the belief that philanthropist Bill Gates has devised a plan to implant microchips in those receiving the vaccine.

3.4 Susceptibility to Misinformation

Exposure to information on social media, political conservatism, older age groups and self-identifying as a minority group were identified as predictors of susceptibility to misinformation in a study designed to investigate coronavirus-related misinformation and its influence on key health-related behaviours. Trust in scientists, getting information from WHO, and high numeracy skills reduce susceptibility to misinformation. Increased susceptibility to misinformation was found to negatively affect self-reported compliance with public health guidance about COVID-19, as well as willingness to get vaccinated against the virus and to recommend the vaccine to vulnerable friends and family.

Another cross-sectional study, conducted in Australia, found that support for misinformation about COVID-19 was more prominent in younger age groups, males, those with inadequate health literacy, those with fewer chronic health conditions, and those who spoke who primarily speak a language other than English at home.

Compared to individuals with adequate health literacy, those with inadequate health literacy were significantly more likely to agree with the following statements:

- "Data about the effectiveness of vaccines is often made up"
- "The threat of COVID-19 is greatly exaggerated"
- "Herd immunity would be beneficial for COVID-19 and this fact is covered up"
- "The government restrictions are stronger than what is needed"

The study found that people with lower health literacy were also more likely to endorse misinformed beliefs about COVID-19 and vaccinations (in general) than those with adequate health literacy.

3.5 Development of a Pro-Vaccine Strategy to Improve Vaccine Uptake

Public health depends on public trust, built through genuine community engagement. To improve vaccine uptake, the public health system should be guided by the WHO recommendations on the development of a pro-vaccination strategy that incorporates the following 10 key guidelines summarized in the Table below:

Table 1: Summary of the WHO Key Guidelines that should comprise a Pro-Vaccination Strategy

Core Elements	Summary
1. Behaviour Change Planning	←Systematic approach to planning, including identifying objectives, design processes, and monitoring and evaluation. ←Strong leadership (see Appendix 2 for examples of planning models and guides for vaccine promotion efforts)

Core Elements	Summary
2. Audience targeting and segmentation	←Targeted approach that uses a different intervention mix for different subsets of the population—Insight' data about citizens' attitudes, beliefs, wants, and behaviours should inform interventions. ←Identify and understand what will prevent, encourage, and assist vaccine uptake. ←Focus on the unprotected and under protected population groups such as: 'The hesitant', 'The unconcerned', 'The poorly reached' and 'The active resisters'.
3. Competition and barrier analysis and action	←Reduce the impact of four kinds of competition: 1) active competition from the anti-vaccination movement. 2) passive competition in the form of inaccurate media coverage. 3) competition from negative social norms and; 4) competition in the form of structural and economic factors.
4. Mobilization	← Build and sustain coalitions of organizations and individuals who can assist through the provision of resources, expertise, credibility, and access. Critical asset identification and management falls into three main categories: 1) government capacity coordination, 2) private sector and NGO sector mobilization, and 3) the mobilization of civil society.
5. Vaccine demand building	←Evidence-based, and theory-informed health communication and health marketing that incorporates the application of behavioural science techniques. ←Conduct formative research including secondary research based on published literature and case studies and primary research with interviews and surveys in each population to gain audience-specific insights.
6. Community engagement	←Ongoing community engagement and trust-building programs. Programs should be focused on confidence-building and active hesitancy prevention, together with regular national assessments of population concern and trust. ←Transparency regarding vaccine licensing, manufacture, and prioritization planning
7. Vaccine access	←Coordinated mix of interventions to promote vaccine access not limited to media and community advocates. ←Explain reasoning for the prioritization models. ←Develop and share schedules and timetables for total population vaccination before vaccination roll out begins so that everyone understands when they will get access. ←Share plans for vaccine rollout prior to availability so that there is time for ethical and procedural issues to be publicly debated and a consensus reached.
8. Marketing promotions strategy	←Tailored messages focusing on known motivators for specific groups are more likely to produce a desired behavioural response than a 'one size fits all' approach. To produce tailored messages, we recommend quantitative and qualitative formative research and ascertaining the efficacy of strategies with pre-test research before launch. ←Familiarity and trust in the messenger, as well as the message, is also a crucial success feature in tackling vaccine hesitancy.
9. News media relations and outreach	←Proactive strategy for working with traditional media - - proactive, rolling media briefings, story generation, editorial feeds, facilitating access to medical and other clinical and public health experts, advisers, and data. ←24/7 media monitoring and rebuttal/correction systems.
10. Digital media strategy	←Develop a dialogue and joint strategy with social media platform providers to review and action against anti-vaccination misinformation and vaccine hesitancy promotion. Governments and regional bodies should convince or regulate platform providers to remove misinformation. ←Build a proactive COVID-19 vaccine trust capacity for active engagement in the social media space as part of the overall promotional strategy. ←Develop and support continuous positive story streams, nurturing multiple supportive voices, and amplification of pro-vaccination grassroots advocates. ←Dedicate staff to support pro-vaccine influencers, advocates, and social networks. ←Identify and respond to false social media posts instantly to prevent the decline of trust in public health authorities.

3.6 Next Steps

As the Ministry of Health, Trinidad and Tobago prepares to roll-out its vaccination programme/campaign, the following key next steps must be given consideration:

- Partner with academic institutions to conduct of formative, primary research, and secondary research (key informant interviews, focus groups, surveys with different population groups).
- Convene a multi-stakeholder committee/task force/working group to develop and implement a tailored pro-vaccination strategy for Trinidad and Tobago.
- Develop a detailed, realistic workplan with clear timelines.
- Develop a monitoring and evaluation plan to assess the impact of the 10 key guidelines in Table 1

Vaccine hesitancy should be addressed early to prevent disruptions to immunization programme. Public health officials responsible for vaccination programmes/campaigns must pay close attention to vaccine concerns and be responsive to address public anxiety and distrust of vaccines and vaccine programme. Provider–parent communication should involve participatory language.

4. Vaccine Safety and Efficacy in Children, the Elderly and Other Groups

4.1 Background

Many children have been infected with this virus since the beginning of the pandemic, and children have suffered in numerous other ways. This includes disruptions to their education, mental and emotional health, and diminished access to medical services.

In Trinidad, we had over 20 COVID MIS-C (Multisystem Inflammatory Syndrome in Children) cases. A few of them had severe disease with reduced cardiac function requiring ICU care and many had coronary artery disease with unknown long-term prognosis. There were also a few ADEM (Acute disseminated encephalomyelitis) cases affecting the brain and spinal cord. These appear to represent a higher number of severe disease cases in children than other Caribbean islands.

In the current COVAX agreement, children under 16 years are not included. While children are not considered to be the most vulnerable to the effects of severe COVID infection, vaccinating them will help prevent the spread of the virus and achieve herd immunity and protect the older vulnerable sub populations. Children also need to return to school and engage society Face-to-Face. Despite controversy concerning benefits, routine immunization of children with existing programmes should be encouraged at this time.

A National Academy of Medicine panel that crafted a plan for prioritizing vaccine distribution in the US included children in its third of four phases. The committee advises that only those children at very high risk of exposure and serious outcomes should be prioritized for vaccination, but it is unlikely in this roll-out phase.

CITAG (Caribbean Immunization Technical advisory group) and PAHO have recently met to plan the rollout of toolkits and guidance documents for vaccine acceptance in the Caribbean which include advice on children. In addition to dose adjustments in younger children we will need to consider our paediatric sub populations separately especially our immunocompromised, sickle cell population and those in residential care.

4.2 Covid-19 Vaccines in Children

Vaccines have not been tested on children under 16 years and there is no safety and efficacy data on vaccination in younger children, at this time.

Pfizer BioNTech SE became the first Covid-19 vaccine developers to include children in U.S. trials in September. Moderna Inc., whose vaccine has also shown to be effective in adults, began a trial for children 12 to17 years old. In the AstraZeneca/Oxford trials, in the 5-12year-old subgroup was recently removed. It does not appear that the schedule of COVID-19 vaccine doses will be different for children, but that could change as testing goes on.

Dr. Paul A. Offit, a vaccine expert at Children's Hospital of Philadelphia, said that vaccines "for the most part" work equally well in children and adults. Occasionally, as with the hepatitis B vaccine, different doses are required, he said. Moderna will study the same dose in children that it has tested in adults and also plans to use its adult schedule – two doses four weeks apart – in an upcoming trial with 3,000 adolescents. Pfizer's vaccine is being tested in adolescents with a two-dose series, three weeks apart, like in adults.

4.3 Breast-Feeding Women

There are no data yet on the safety and efficacy of COVID-19 vaccines in infants of breast-feeding mothers, but no specific contraindication is known.

4.4 Pregnant Women

There are no data yet on the safety and efficacy of COVID-19 vaccines in pregnancy. Given the lack of evidence a precautionary approach is favoured and does not currently advise COVID-19 vaccination in pregnancy.

4.5 Demographic, Socioeconomic Factors, Co-Morbidities and Covid-19 Vaccine

Subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across age groups, genders, racial and ethnic groups, and participants with medical comorbidities associated with high risk of severe COVID-19.

The Pfizer and BioNTech covid-19 vaccine study showed that seven days after the second dose, vaccine efficacy ranged from 89% to 100% across subgroups defined by age, sex, race, ethnicity, baseline body mass index, and the presence of coexisting conditions.

By Gender
Although generally women exhibit a greater immune response that can facilitate vaccine efficacy, in Covid-19 Vaccine studies no disaggregation had been done by gender to date.

Socio-economic and Ethnicity
This has not yet been determined. We know that COVID-19 disproportionately affects people of lower economic status and vaccine acceptance is also lower in this group. Both Moderna and Pfizer reported about 9% African people in vaccinated groups in trials. Studies have shown similar efficacy racial and ethnic groups, but no data exists that is currently disaggregated by socioeconomic status.

In the elderly
The impact of aging and the concept of immunosenescence is particularly relevant within the context of the COVID-19 pandemic. The effectiveness of vaccination is often reduced due to *immunosenescence and* COVID-19 vaccines efficacy in older adults is still of concern. Sanofi and GSK recently announced a delay in adjuvanted recombinant protein -based COVID-19 vaccine to improve response in the elderly.

Pfizer/BioNTech vaccine data indicates high efficacy in all age groups (16 years and over) including encouraging results in older adults but has not specifically stated the difference in elderly. Moderna reported a small decrease in efficacy to 86% in over 65 age group compared to 94% overall.

Co-morbidities
This is still ongoing, the evidence in insufficient to draw a conclusion. Moderna reported percentages of co-morbidities and obesity. Pfizer will report separately regarding their HIV population.

5. Bibliography

Covid-19 Approved Vaccines, Ongoing Trials And In Special Groups

Published Papers

- Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, Diemert D., for the COVE Study Group* Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2020 Dec 30: DOI: 10.1056/NEJMoa2035389.
- Dan-Yu Lin DZ, Devan V. Mehrotra, Lawrence Corey, Peter B. Gilbert. Evaluating the Efficacy of COVID-19 Vaccines. Available at: https://www.medrxiv.org/content/10.1101/2020.10.02.20205906v2.full
- Ella R, Mohan K, Jogdand H, Prasad S, Reddy S, Sarangi VK, et al. Safety and immunogenicity trial of an inactivated SARS-CoV-2 vaccine-BBV152: a phase 1, double-blind, randomised control trial. medRxiv. 2020. medRxiv 2020.12.11.20210419; doi: https://doi.org/10.1101/2020.12.11.20210419.
- FDA Briefing Document. Moderna COVID-19 Vaccine Available from: https://www.fda.gov/media/144434/download [Accessed 22nd December 2020].
- Greenwood B. The contribution of vaccination to global health: past, present and future. Philosophical Transactions of the Royal Society B: Biological Sciences. 2014;369(1645):20130433.
- Guebre-Xabier M, Patel N, Tian J-H, Zhou B, Maciejewski S, Lam K, et al. NVX-CoV2373 vaccine protects cynomolgus macaque upper and lower airways against SARS-CoV-2 challenge. Vaccine. 2020;38(50):7892-6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7584426/
- Hodgson SH, Mansatta K, Mallett G, Harris V, Emary KR, Pollard AJ. What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2. The lancet infectious diseases. 2020. Published: October 27, 2020DOI: https://doi.org/10.1016/S1473-3099(20)30773-8.
- Keech C, Albert G, Cho I, Robertson A, Reed P, Neal S, et al. Phase 1-2 trial of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine. N Engl Med J 2020:383:2320-2332. Doi: 10.1056/NEJMao20236920. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa2026920?query=featured_home
- Logunov DY, Dolzhikova IV, Zubkova OV, Tukhvatullin AI, Shcheblyakov DV, Dzharullaeva AS, et al. 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. 2020;396(10255):887-97. Available from: https://www.sciencedirect.com/science/article/pii/S0140673620318663?via%3Dihub
- Mahase E. Covid-19: Pfizer vaccine efficacy was 52% after first dose and 95% after second dose, paper shows. British Medical Journal Publishing Group; 2020; 371:m4826. doi: https://doi.org/10.1136/bmj.m4826
- McCartney PR. Sex-Based Vaccine Response in the Context of COVID-19. Journal of Obstetric, Gynecologic & Neonatal Nursing. 2020;49(5):405-8. Published online 2020 Aug 5. doi: 10.1016/j.jogn.2020.08.001
- Moderna COVID-19 Vaccine VRBPAC Briefing Document *BMJ* 2020; 371:m4826 doi: https://doi.org/10.1136/bmj.m4826 (Published 11 December 2020).https://www.ox.ac.uk/news/2020-12-08-first-peer-reviewed-results-phase-3-human-trials-oxford-coronavirus-vaccine
- Modjarrad K, Roberts CC, Mills KT, Castellano AR, Paolino K, Muthumani K, et al. Safety and immunogenicity of an anti-Middle East respiratory syndrome coronavirus DNA vaccine: a phase 1, open-label, single-arm, dose-escalation trial. The Lancet Infectious Diseases. 2019;19(9):1013-22.
- Osada T, Yang XY, Hartman ZC, Glass O, Hodges BL, Niedzwiecki D, et al. Optimization of vaccine responses with an E1, E2b and E3-deleted Ad5 vector circumvents pre-existing anti-vector immunity. Cancer gene therapy. 2009;16(9):673-82. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3800002/
- Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, Perez JL; C4591001 Clinical Trial Group. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020 Dec 10: NEJMoa2034577. doi: 10.1056/NEJMoa2034577.
- Ramasamy MN, Minassian AM, Ewer KJ, Flaxman AL, Folegatti PM, Owens DR, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. The Lancet. 2020. Available at: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32466-1/fulltext
- Schenkelberg T. Vaccine-induced protection in aging adults and pandemic response. Biochemical and Biophysical Research Communications. 2020. Nov 17 doi: 10.1016/j.bbrc.2020.10.090

- Serra LC, York LJ, Balmer P, Webber C. Meningococcal group A, C, W, and Y tetanus toxoid conjugate vaccine: a review of clinical data in adolescents. Journal of Adolescent Health. 2018;63(3):269-79. Available at: https://www.jahonline.org/article/S1054-139X(18)30193-9/fulltext
- Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. The Lancet. 2020. Available at: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32661-1/fulltext
- Wang H, Zhang Y, Huang B, Deng W, Quan Y, Wang W, et al. Development of an inactivated vaccine candidate, BBIBP-CorV, with potent protection against SARS-CoV-2. Cell. 2020;182(3):713-21. e9. DOI:https://doi.org/10.1016/j.cell.2020.06.008
- Xia S, Duan K, Zhang Y, Zhao D, Zhang H, Xie Z, et al. Effect of an inactivated vaccine against SARS-CoV-2 on safety and immunogenicity outcomes: interim analysis of 2 randomized clinical trials. Jama. 2020;324(10):951-60. doi:10.1001/jama.2020.15543
- Zhang Y, Zeng G, Pan H, Li C, Hu Y, Chu K, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. The Lancet Infectious Diseases. 2020. Nov 17. pii: S1473-3099(20)30843-4. doi: 10.1016/S1473-3099(20)30843-4.
- Zhu FC, Guan XH, Li YH, Huang JY, Jiang T, Hou LH, Li JX, Yang BF, Wang L, Wang WJ, Wu SP, Wang Z, Wu XH, Xu JJ, Zhang Z, Jia SY, Wang BS, Hu Y, Liu JJ, Zhang J, Qian XA, Li Q, Pan HX, Jiang HD, Deng P, Gou JB, Wang XW, Wang XH, Chen W. Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial. Lancet. 2020 Aug 15;396(10249):479-488. doi: 10.1016/S0140-6736(20)31605-6. Epub 2020 Jul 20. PMID: 32702299.

Registered Clinical Trials

- A Clinical Trial of A COVID-19 Vaccine Named Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector). Available from: https://clinicaltrials.gov/ct2/show/NCT04566770 [Accessed 22nd December 2020].
- A Clinical Trial of a Recombinant Adenovirus 5 Vectored COVID-19 Vaccine (Ad5-nCoV) With Two Doses in Healthy Adults. Available from: https://clinicaltrials.gov/ct2/show/NCT04552366 [Accessed 22nd December 2020].
- A Phase 1 Randomised, Double-Blind, Placebo-Controlled, Dosage-Escalation, Single Centre Study To Evaluate The Safety And Immunogenicity Of An Adjuvanted SARS-CoV-2 Sclamp Protein Subunit Vaccine (COVID-19 vaccine) In Healthy Adults Aged 18 To 55 Years Old. Available from: https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=379861&isReview=true [Accessed 22nd December 2020].
- A Phase III clinical trial for inactivated novel coronavirus pneumonia (COVID-19) vaccine (Vero cells). Available from: http://www.chictr.org.cn/showprojen.aspx?proj=56651 [Accessed 22nd December 2020].
- An Event-Driven, Phase 3, Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate the Efficacy, Safety, Immunogenicity, and Lot-to-Lot consistency of BBV152, a Whole virion Inactivated SARS-CoV-2 Vaccine in Adults greater than or equal to 18 Years of Age. Available from: http://ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=48057&EncHid=&userName=sars-cov-2%20vaccine [Accessed 22nd December 2020].
- An interventional study to evaluate the safety and immune response of a vaccine against Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2, the virus that causes COVID-19 infection) when given to healthy adult participants. DOI: https://doi.org/10.1186/ISRCTN51232965 [Accessed 22nd December 2020].
- An Open Study of the Safety, Tolerability and Immunogenicity of "Gam-COVID-Vac Lyo" Vaccine Against COVID-19. Available from: https://clinicaltrials.gov/ct2/show/NCT04437875 [Accessed 22ndDecember 2020].
- An Open Study of the Safety, Tolerability and Immunogenicity of the Drug "Gam-COVID-Vac" Vaccine Against COVID-19. Available from: https://clinicaltrials.gov/ct2/show/NCT04436471 [Accessed 22ndDecember 2020].
- A Phase II Clinical Trial to Evaluate the Recombinant Vaccine for COVID-19 (Adenovirus Vector) (CTII-nCoV). Available from: https://clinicaltrials.gov/ct2/show/NCT04341389 [Accessed 22ndDecember 2020].
- A Phase 2/3, Observer-Blind, Randomized, Controlled Study to Determine the Safety and Immunogenicity of Covishield (COVID-19 Vaccine) in Healthy Indian Adults. Available from: http://ctri.nic.in/Clinicaltrials/showallp.php?mid1=46186&EncHid=&userName=covid-19%20vaccine [Accessed 22nd December 2020].
- A Phase III, Observer-blind, Randomized, Placebo-controlled Study of the Efficacy, Safety and Immunogenicity of SARS-CoV-2 Inactivated Vaccine in Healthy Adults Aged 18-59 Years in Indonesia. Available from: https://www.ina-registry.org/index.php?act=registry_trial_detail&code_trial=16202009080721WXFM0YX [Accessed 22nd December 2020].
- A prospective open label randomised phase-I seamlessly followed by phase-II study to assess the safety, reactogenicity and immunogenicity of Biological E's novel Covid-19 vaccine containing Receptor Binding Domain of SARS-CoV-2 for protection against Covid-19 disease when administered intramuscularly in a two-dose schedule (0, 28D) to healthy volunteers. Available from: http://ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=48329&EncHid=&userName=covid-19%20vaccine [Accessed 22nd December 2020].

- A Study Looking at the Effectiveness and Safety of a COVID-19 Vaccine in South African Adults.Available from: https://clinicaltrials.gov/ct2/show/NCT04533399?term=vaccine&cond=covid-19&draw=7 [Accessed 22nd December 2020].
- A Study Looking at the Efficacy, Immune Response, and Safety of a COVID-19 Vaccine in Adults at Risk for SARS-CoV-2. Available from: https://clinicaltrials.gov/ct2/show/nct04611802 [Accessed 22nd December 2020].
- A Study of Ad26.COV2.S for the Prevention of SARS-CoV-2-mediated COVID-19 in Adults (ENSEMBLE 2). Available from: https://clinicaltrials.gov/ct2/show/NCT04614948 [Accessed 22nd December 2020].
- A Study of Ad26.COV2.S for the Prevention of SARS-CoV-2-Mediated COVID-19 in Adult Participants (ENSEMBLE). Available from: https://clinicaltrials.gov/ct2/show/NCT04505722 [Accessed 22nd December 2020].
- A Study to Evaluate the Safety and Immunogenicity of MVC-COV1901 Against COVID-19 [NCT04487210] https://clinicaltrials.gov/ct2/show/study/NCT04487210?term=vaccine&cond=covid-19&draw=7 [Accessed 22nd December 2020].
- A Study to Evaluate the Safety, Tolerability, and Immunogenicity of UB-612 COVID-19 Vaccine. https://clinicaltrials.gov/ct2/show/NCT04545749?cond=NCT04545749&draw=2&rank=1 [Accessed 22nd December 2020].
- A randomized, double-blind, placebo-controlled phase III clinical trial of the effectiveness and safety of inoculation of recombinant new coronavirus vaccine (CHO cells) in the prevention of COVID-19 in people 18 years and older. http://www.chictr.org.cn/showprojen.aspx?proj=64718 [Accessed December 22nd, 2020].
- A randomized, double-blind, placebo-controlled phase III clinical trial of the effectiveness and safety of inoculation of recombinant new coronavirus vaccine (CHO cells) in the prevention of COVID-19 in people 18 years and older. Available from: http://www.chictr.org.cn/showprojen.aspx?proj=64718 [Accessed 22nd December 2020].
- A randomized, observer-blind, placebo-controlled, Phase I/II study to evaluate the safety, reactogenicity and immunogenicity of Receptor Binding Domain (RBD) SARS-CoV-2 (COVID-19) Hepatitis B surface antigen (HBsAg) virus like particle (VLP) Vaccine in Healthy Adults. Available from: https://anzctr.org.au/Trial/Registration/TrialReview.aspx?id=380145&isReview=true. [Accessed December 22nd, 2020]
- Clinical Study of Recombinant Novel Coronavirus Vaccine.Available from: https://clinicaltrials.gov/ct2/show/NCT04466085?term=NCT04466085&draw=2&rank=1 [Accessed 22nd December 2020].
- Clinical Trial of Efficacy, Safety, and Immunogenicity of Gam-COVID-Vac Vaccine Against COVID-19 in Belarus. Available from: https://clinicaltrials.gov/ct2/show/NCT04564716 [Accessed 22nd December 2020].
- Clinical Trial of Efficacy, Safety, and Immunogenicity of Gam-COVID-Vac Vaccine Against COVID-19 (RESIST). Available from: https://clinicaltrials.gov/ct2/show/NCT04530396 [Accessed 22nd December 2020].
- Clinical Trial of the Immunogenicity, Safety, and Efficacy of the Gam-COVID-Vac Vaccine Against COVID-19 in Venezuela (VENEZUELA). Available from: https://clinicaltrials.gov/ct2/show/NCT04642339 [Accessed 22nd December 2020].
- Clinical Trial of Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) Against COVID-19. Available from: https://clinicaltrials.gov/ct2/show/NCT04540419 [Accessed 22nd December 2020].
- Clinical Trial to Assess Safety and Immunogenicity of Gam-COVID-Vac Combined Vector Vaccine for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection. Available from: https://clinicaltrials.gov/ct2/show/NCT04640233 [Accessed 22nd December 2020].
- Evaluation of the Safety and Immunogenicity of a SARS-CoV-2 rS Nanoparticle Vaccine With/Without Matrix-M Adjuvant. Available from: https://clinicaltrials.gov/ct2/show/NCT04368988?draw=2 [Accessed 22nd December 2020].
- First patient dosed in COVID-19 vaccine tablet clinical trial. Available from: https://www.europeanpharmaceuticalreview.com/news/130177/first-patient-dosed-in-covid-19-vaccine-tablet-clinical-trial/ [Accessed 22nd December 2020].
- GRAd-COV2 Vaccine Against COVID-19. Available from: https://clinicaltrials.gov/ct2/show/NCT04528641?term=vaccine&cond=covid-19&draw=8. [Accessed 22nd December 2020].
- KBP-201 COVID-19 vaccine trial in healthy volunteers. Available from: https://clinicaltrials.gov/ct2/show/study/NCT04473690?term=vaccine&cond=covid-19&draw=3 [Accessed 22nd December 2020].
- Monovalent recombinant COVID19 vaccine. Available from: https://clinicaltrials.gov/ct2/show/nct04453852?term=vaccine&cond=covid-19&draw=5. [Accessed 22nd December 2020].
- Phase I Clinical Study of Recombinant Novel Coronavirus Vaccine. Available from: https://clinicaltrials.gov/ct2/show/nct04445194?term=longcom&draw=2 [Accessed 22nd December 2020].
- Phase I Trial of a Recombinant COVID-19 Vaccine (CHO Cell). Available from: https://clinicaltrials.gov/ct2/show/NCT04636333 [Accessed 22nd December 2020].
- Phase I study, open, sequential and adaptive, to evaluate the safety, reactogenicity and explore immunogenicity, of the PROphylactic Vaccine Candidate FINLAY- FR-2 anti SARS-CoV-2 (COVID-19). https://rpcec.sld.cu/ensayos/RPCEC00000340-Sp [Accessed 22nd December 2020].
- Phase I/II study, randomized, controlled, adaptive, double-blind and multicenter to evaluate the safety, reactogenicity and immunogenicity of the PROphylactic Vaccine Candidate FINLAY- FR-1 anti SARS – CoV – 2 in a two-dose scheme. (COVID-19). SOBERANA 01 | Registro Público Cubano de Ensayos Clínicos (sld.cu). [Accessed 22nd December 2020].

- Phase III Trial of A COVID-19 Vaccine of Adenovirus Vector in Adults 18 Years Old and Above. Available from: https://clinicaltrials.gov/ct2/show/NCT04526990 [Accessed 22nd December 2020].
- Randomized, double-blinded, placebo parallel-controlled phase III clinical trial to evaluate the Immunogenicity and safety of the inactivated SARS-CoV-2 Vaccine (Vero cell) in healthy population aged 18 years and above Available from: http://www.chictr.org.cn/showprojen.aspx?proj=62581 [Accessed 22nd December 2020].
- Recombinant New Coronavirus Vaccine (CHO Cells) to Prevent SARS-CoV-2 Phase I Clinical Trial (≥60 Years Old). Available from: https://clinicaltrials.gov/ct2/show/study/NCT04550351?term=vaccine&cond=covid-19&draw=13 [Accessed 22nd December 2020].
- Safety and Immunogenicity of COVI-VAC, a Live Attenuated Vaccine Against COVID-19. Available from: https://clinicaltrials.gov/ct2/show/NCT04619628 [Accessed December 22nd, 2020].
- Safety and Immunogenicity Trial of an Oral SARS-CoV-2 Vaccine (VXA-CoV2-1) for Prevention of COVID-19 in Healthy Adults. Available from: https://clinicaltrials.gov/ct2/show/NCT04563702. [Accessed 22nd December 2020].
- Safety and Immunogenicity Trial of Multi-peptide Vaccination to Prevent COVID-19 Infection in Adults (pVAC) https://clinicaltrials.gov/ct2/show/NCT04546841?term=vaccine&cond=covid-19&draw=2&rank=1. [Accessed 22nd December 2020].
- Safety, Tolerability and Immunogenicinity of a Coronavirus-Like Particle COVID-19 Vaccine in Adults Aged 18-55. Available from: Years. https://clinicaltrials.gov/ct2/show/NCT04450004?term=vaccine&cond=covid-19&draw=2 [Accessed December 22nd, 2020].
- Safety, Tolerability and Immunogenicity of the Candidate Vaccine MVA-SARS-2-S Against COVID-19. Available from: https://clinicaltrials.gov/ct2/show/NCT04569383 [Accessed 22nd December 2020].
- SCB-2019 as COVID-19 Vaccine. Available from: https://clinicaltrials.gov/ct2/show/nct04405908?term=clover&cond=covid-19&draw=2 [Accessed 22nd December 2020].
- Sex-Based Vaccine Response in the Context of COVID-19 J Obstet Gynecol Neonatal Nurs. 2020 Sep; 49(5): 405–408. Published online 2020 Aug 5. doi: 10.1016/j.jogn.2020.08.001.
- Study of the Safety of Prophylactic Vaccination With 2nd Generation E1/E2B/E3-Deleted Adenoviral-COVID-19 in Normal Healthy Volunteers. Available from: https://clinicaltrials.gov/ct2/show/NCT04591717 [Accessed 22nd December 2020].
- Study of the Safety, Reactogenicity and Immunogenicity of "EpiVacCorona" Vaccine for the Prevention of COVID-19 (EpiVacCorona). https://clinicaltrials.gov/ct2/show/NCT04527575 [Accessed 22nd December 2020].
- Study of Recombinant Protein Vaccine Formulations Against COVID-19 in Healthy Adults 18 Years of Age and Older. Available from: https://clinicaltrials.gov/ct2/show/nct04537208?term=sanofi&cond=sars-cov-2&draw=2 [Accessed 22nd December 2020].
- The Study of "Gam-COVID-Vac" Vaccine Against COVID-19 With the Participation of Volunteers of 60 y.o and Older. Available from: https://clinicaltrials.gov/ct2/show/NCT04587219 [Accessed 22nd December 2020].
- Vaccine-induced protection in aging adults and pandemic response Biochem Biophys Res Commun. 2020 Nov 17 doi: 10.1016/j.bbrc.2020.10.090
- Vaxart VXA-CoV2-1 COVID-19 Oral Vaccine Description. Available from: https://www.precisionvaccinations.com/vaccines/vaxart-covid-19-oral-vaccine. [Accessed 22nd December 2020].
- What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2 Susanne H Hodgson, Kushal Mansatta, Garry Mallett, Victoria Harris, Katherine R W Emary, Andrew J Pollard. Lancet Review, Published: October 27, 2020DOI: https://doi.org/10.1016/S1473-3099(20)30773-8
- WHO Draft landscape of COVID-19 candidate vaccines. 2020. Available from: WH. DRAFT landscape of COVID-19 candidate vaccines. [Accessed 22nd December 2020].

In The Media

- COVAXX Announces $2.8 Billion in Advance Purchase Commitments to Deliver More Than 140 Million Vaccine Doses to Emerging Countries.Available from: https://www.businesswire.com/news/home/20201125005466/en/COVAXX-Announces-2.8-Billion-in-Advance-Purchase-Commitments-to-Deliver-More-Than-140-Million-Vaccine-Doses-to-Emerging-Countries [Accessed December 22nd, 2020].
- Covid-19: Oxford-AstraZeneca vaccine approved for use in UK - BBC News. [Accessed 30th December 2020].
- Cuba joins the race for vaccine against the coronavirus. Available from: https://www.dw.com/en/cuba-joins-the-race-for-vaccine-against-the-coronavirus/a-54615364 [Accessed 22nd December 2020].
- Cuba to begin clinical trials of COVID-19 vaccine. Vaccine 'a priority for our entire science and innovation system at BioCubaFarma,' says company head. Available from: https://www.aa.com.tr/en/americas/cuba-to-begin-clinical-trials-of-covid-19-vaccine-/1947388 [Accessed December 22nd, 2020].
- First peer-reviewed results of phase 3 human trials of Oxford coronavirus vaccine demonstrate efficacy. Available from: https://www.ox.ac.uk/news/2020-12-08-first-peer-reviewed-results-phase-3-human-trials-oxford-coronavirus-vaccine. [Accessed 22nd December 2020].

- It won't be rolled out for COVID-19, but technology developed for UQ vaccine might help fight future viruses. December 13th. Available from: https://www.abc.net.au/news/health/2020-12-14/how-the-uq-vaccine-might-help-fight-other-disease-threats/12979242. [Accessed December 22nd, 2020].
- Medigen says ready to produce vaccines next year. Taipei Times. Available from: https://www.taipeitimes.com/News/biz/archives/2020/11/04/2003746299 [Accessed December 22, 2020].
- Medigen Signs Agreement with Metronic, Making it the First Taiwan-made Vaccine Deal.Available from: https://geneonline.news/en/2020/11/26/medigen-signs-agreement-with-metronic-making-it-the-first-taiwan-made-vaccine-deal/ [Accessed 22nd December 2020].
- Russia begins mass trials of second coronavirus vaccine. Available from: https://www.reuters.com/article/us-health-coronavirus-russia-cases-idUSKBN28A0P0 [Accessed 22nd December 2020].
- Serum Institute of India stops clinical trial of Oxford-AstraZeneca COVID-19 Vaccine. Available from: https://english.lokmat.com/health/serum-institute-of-india-stops-clinical-trials-of-oxford-astrazeneca-covid-19-vaccine/ [Accessed 22nd December 2020].
- Serum Institute rejects charges by Covid-19 vaccine trial participant of 'serious side effects'.Available from: https://indianexpress.com/article/india/covishield-vaccine-trial-participant-alleges-neuro-breakdown-impaired-cognitive-functions-7073013/ [Accessed 22nd December 2020].

Beliefs and Misconceptions about COVID-19 Vaccines and Strategies to Improve Vaccine Uptake in the Public Health Care System

- Bonn D. T&T is ready for the Covid vaccine. Trinidad Express [Internet]. 2020 Nov 30 [cited 2020 Dec 14]; Available from: https://trinidadexpress.com/newsextra/t-t-is-ready-for-the-covid-vaccine/article_89ab5f46-333c-11eb-beb3-0f833210c34c.html
- Coronavirus: 5G and microchip conspiracies around the world. BBC News [Internet]. 2020 Jun 26 [cited 2020 Dec 17]; Available from: https://www.bbc.com/news/53191523
- Figueiredo A de, Simas C, Karafillakis E, Paterson P, Larson HJ. Mapping global trends in vaccine confidence and investigating barriers to vaccine uptake: a large-scale retrospective temporal modelling study. The Lancet. 2020 Sep 26;396(10255):898–908.
- French J, Deshpande S, Evans W, Obregon R. Key Guidelines in Developing a Pre-Emptive COVID-19 Vaccination Uptake Promotion Strategy. Int J Environ Res Public Health [Internet]. 2020 Aug [cited 2020 Dec 15];17(16). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7459701/
- How Bill Gates became the voodoo doll of Covid conspiracies. BBC News [Internet]. 2020 Jun 5 [cited 2020 Dec 17]; Available from: https://www.bbc.com/news/technology-52833706
- Hussain S. Why are some Muslims suspicious of a COVID-19 vaccine? [Internet]. ABC Religion & Ethics. Australian Broadcasting Corporation; 2020 [cited 2020 Dec 17]. Available from: https://www.abc.net.au/religion/overcoming-muslim-reticence-toward-covid-vaccine/12927958
- McCaffery K, Dodd R, Cvejic E, Ayre J, Isautier J, Copp T, et al. Health literacy and disparities in COVID-19–related knowledge, attitudes, beliefs and behaviours in Australia. Public Health Res Pract [Internet]. 2020 [cited 2020 Dec 15];30(4). Available from: https://www.phrp.com.au/?p=39821
- Programs JHC for C. KAP COVID Study Methods [Internet]. Johns Hopkins Center for Communication Programs. [cited 2020 Dec 18]. Available from: https://ccp.jhu.edu/kap-covid/kap-covid-study-methods/
- Roozenbeek J, Schneider CR, Dryhurst S, Kerr J, Freeman ALJ, Recchia G, et al. Susceptibility to misinformation about COVID-19 around the world. R Soc Open Sci [Internet]. 2020 Oct 14 [cited 2020 Dec 15];7(10). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7657933/
- Smith TC, Reiss DR. Digging the rabbit hole, COVID-19 edition: anti-vaccine themes and the discourse around COVID-19. Microbes Infect. 2020;22(10):608–10.
- Sze S, Pan D, Nevill CR, Gray LJ, Martin CA, Nazareth J, et al. Ethnicity and clinical outcomes in COVID-19: A systematic review and meta-analysis. EClinicalMedicine [Internet]. 2020 Dec 1 [cited 2020 Dec 17];29. Available from: https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30374-6/abstract
- TV I. Vaccines and Immunity Conference [Internet]. 2020 [cited 2020 Dec 18]. Available from: https://vimeo.com/484531890
- Vaccine rumours debunked: Microchips, 'altered DNA' and more. BBC News [Internet]. 2020 Dec 2 [cited 2020 Dec 17]; Available from: https://www.bbc.com/news/54893437
- World Health Organization. COVAX: The vaccines pillar of the access to COVID-19 tools (ACT) Accelerator [Internet]. Geneva, Switzerland: World Health Organization; 2002 Nov [cited 2020 Dec 14] p. 29. Available from: https://www.who.int/publications/m/item/covax-the-vaccines-pillar-of-the-access-to-covid-19-tools-(act)-accelerator

6. Appendices

6.1 APPENDIX 1: Platform-Based Narratives of Ongoing and Recruiting Vaccine Trials

6.1.1 Non-Replicating Viral Vector Vaccines

Non-replicating viral vaccine vectors have been previously researched and are well-established in vaccine technology. The advantages of eliciting a heightened immune response, along with its genetic stability, lack of integration into the host genome and the ability to be grown in high titres indicate why more than twenty (20) scientific teams are using them to establish a vaccine against SARS-CoV-2. Many of these studies are still in the preliminary stages or Phase 1 but there are some candidates that have published data from Phase1/2 and Phase 3. It should be noted that one of the disadvantages in utilising these vectors, especially adenoviruses, is the possibility of prior immunity against them. Researchers must present solutions to overcome this obstacle or show that the immune responses generated are not affected by that possibility.

I. VACCINE NAME: AD5-NCOV

MANUFACTURER: Institute of Biotechnology, Academy of Military Medical Sciences, PLA of China collaborating with CanSino Biologics Inc., Jiangsu Province Centers for Disease Control and Prevention, Hubei Provincial Center for Disease Control and Prevention and Zhongnan Hospital.

VACCINE PLATFORM: Adenovirus type 5 vector (Ad5-nCoV) which encodes for a full-length spike (S) protein of SARS-CoV-2.

TRIAL REGISTRATION #: NCT04398147, NCT04313127, NCT04568811, NCT04398147, NCT04341389, NCT04566770, NCT04540419,NCT04526990

AVAILABILITY: Not yet available.

BRIEF SUMMARY:

Phase 1 trial (completed, March 2020). Single-centered, open-label, non-randomized, dose-escalating (5 x 10^{10}, 1 x 10^{11} and 1.5 x 10^{11} viral particles).

Phase 2 trial (started 12th April 2020, proposed completion date 31st January 2021). A randomized, double-blinded and placebo-controlled trial in healthy participants, 18 years and older. Mean age was 39.7 years [range 18-83 years; 61% between 18 – 44 years; 26% between 45 – 54 years and 13% over 55 years]. 50% males. Single dose given and participants were monitored for 30 minutes post injection.

Trial included 508 participants: 253 given 1 x 10^{11} dose, 129 given 5 x 10^{11} dose and 126 given placebo.

OUTCOMES MEASUREMENTS:

To evaluate immunogenicity and safety of Ad5-nCoV vaccine. Immunogenicity was tested on days 0, 14, 28 post-vaccination with continued testing 6 months after vaccination.

Safety: High dose was associated with increased risk of more severe AEs.

Overall quality of evidence: Level III/Low Grade/High risk of bias

The Phase 1 trial was open-label, non-controlled and non-randomized.

Duration of protection: Unknown.

SUMMARY STATEMENT:

Phase 2 is presently ongoing in Argentina, Chile, Mexico, Pakistan and Russia, which although more ethnically diverse may not fully represent ethnic groups in the Caribbean. Another concern is the presence of Anti-Ad5 immunity, which the authors recognized differs regionally throughout the world and could affect vaccine efficacy. Encouragingly, studies are underway with regards to this vaccine and participants less than 18 years of age. This data can only assist along with data from assessments 6 months post-vaccination.

II. VACCINE NAME: AD5-NCOV

MANUFACTURER: Institute of Biotechnology, Academy of Military Medical Sciences, PLA of China collaborating with Zhongnan Hospital.

VACCINE PLATFORM: Recombinant adenovirus 5 vectored COVID-19 vaccine (Ad5-nCoV)

AVAILABILITY: Not available. Phase I Study to start date on 29th September 2020. Proposed primary completion date, 31st December 2020 and proposed study completion, 30th June 2021.

BRIEF SUMMARY:

Non-randomized study with 168 participants, 18 years and older, utilizing two doses of vaccine administered via two different routes. Participants divided into 6 groups:

A - IM – n =24 – 5 x 10^{10} VP on day 0 and day 56.

B – Mixed – n = 24 – day 0= IM 5 x 10^{10} VP; day 28 = mucosal 2 x 10^{10} VP

C – Mucosal – n = 24 – 2 x 10^{10} VP on day 0 and day 28

D – Mucosal – n = 24 - 1 x 10^{10} VP on day 0 and day 28

E – IM – n = 24 - 5 x 10^{10} VP on day 0

F – IM – n = 24 – Two doses on left & right arms of 5 x 10^{10} VP on day 0

All genders accepted

SAFETY: NOT KNOWN.

OVERALL QUALITY OF EVIDENCE: NOT KNOWN.

III. VACCINE NAME: GRAD-COV-2

MANUFACTURER: ReiThera Srl collaborating with Istituto Nazionale per le Malattie Infettive Lazzaro Spallanzani (National Institute of Infectious Diseases – Italy)

VACCINE PLATFORM: Replication defective Gorilla adenovirus encodes for SARS-CoV-2 full length Spike protein.

TRIAL REGISTRATION #: NCT04528641

AVAILABILITY: Not available. In Phase I trial started 10th August 2020, projected study completion date: 31st July 2021.

BRIEF SUMMARY:

Evaluation of a single intramuscular injection of GRAd-COV2 at varying dosage levels: 5 x 10^{10}, 1 x 10^{11} and 2 x 10^{11} viral particles. 90 healthy individuals divided into age groups: 18-55 years and 65-85 years.

Evaluations: Day 2, Wk 1, 2, 4, 8, 12, 24 post-immunisation

Study is non-randomised

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: NOT KNOWN.

IV. VACCINE NAME: VXA-COV2-1 – ORAL VACCINE

MANUFACTURER: Vaxart

VACCINE PLATFORM: Non-replicating Ad5 vector adjuvatned oral tableted vaccine.

TRIAL REGISTRATION #: NCT04563702

AVAILABILITY: Not available. Phase 1 started 21st September 2020; projected primary completion date, 10th December 2020; projected study completion date, October 2021.

BRIEF SUMMARY:

Non-randomized study with repeat dosing and dose ranging. 35 Participants, 18 – 54 years old, males and females included. No participants with HIV, hypersensitivities, SARS-CoV-2 infection and other clinical conditions allowed.

Participants divided into two cohorts. One will receive the low dose – 1 x 10^{10} IU at day 1; a subset will receive a second dose at day 29. The second cohort will receive the high dose – 1 x 10^{11} at day 29.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

Note: Of particular interest is the delivery of the vaccine in an oral formulation.

V. VACCINE NAME: SPUTNIK V/GAM-COVID-VAC

MANUFACTURER: Dr. Reddy's Laboratories Ltd collaborating with Gamaleya Research Institute of Epidemiology and Microbiology, Health Ministry of the Russian Federation, RDIF (Russian Direct Investment Fund) and JSS Medical Research India Pvt. Ltd.

VACCINE PLATFORM: non-replicating recombinant human adenovirus vectors (DNA), both carrying the gene for the SARS-CoV-2 full length glycoprotein S: adenovirus type 26 (rAd26-S) and adenovirus type 5 (rAd5-S) vectors.

AVAILABILITY: Not available. Phase 2/3 study to start in December 2020, proposed primary completion date, August 2021; proposed study completion date: September 2021.

BRIEF SUMMARY:

Randomized, double-blind, placebo-controlled, parallel group, multi-centered study in 1600 healthy Indian participants, 18 years and older and both genders. The Phase 3 of this study is occurring in India, Belarus, Russia and Venezuela with variances in participants' numbers and age grouping. At this time, little is known regarding participant demographics. Of note, the lyophilized version is not being tested.

Phase 2: 100 participants to be enrolled in 3:1 (Investigational Medicinal Product (IMP): Placebo) ratio. After injection, assessment will be done till day 28 and continued till day 180.

Phase 3: 1500 participants to be enrolled and randomized in the ratio of 3:1 (Vaccine: Placebo)

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE NOT KNOWN.

VI. VACCINE NAME: ADENOVIRUS TYPE 5 VECTOR /AD5-NCOV

MANUFACTURER: CanSino Biologics collaborating with Beijing Institute of Biotechnology and Jiangsu Province Centers for Disease Control and Prevention

VACCINE PLATFORM: An Adenovirus Type 5 Vector

AVAILABILITY: Not available. Phase 2 study started on 24th September 2020; proposed primary completion date, 21st August 2021; proposed study completion date, 20th October 2022.

BRIEF SUMMARY:

A Randomized, Double-blind, Placebo -Controlled Phase IIb study evaluating safety and immunogenicity of Ad5-nCoV in participants 6 years and older and those previously vaccinated with Ad5-EBOV. The addition of children and teenagers into the vaccine trials will give much needed information regarding protection for this subpopulation.

Intramuscular injections will be either experimental vaccine or placebo. Participants will be subdivided as follows:

MID A: n=20 (18-49 yrs) IM, 2 doses - Ad5-nCoV

MID B: n=10 (18-49 yrs) IM, 2 doses – Ad5-nCoV-placebo

MIN A: n=100 (6 – 17 yrs) IM, 2 doses - Ad5-nCoV

MIN B: n=50 (6 – 17yrs) IM, 2 doses – Ad5-nCoV-placebo

OLD A: n= 100 (56 yrs and above) 2 doses (Low dose) - Ad5-nCoV

OLD B: n= 100 (56 yrs and above) 2 doses (Middle dose) - Ad5-nCoV

OLD C: n=50 (56 yrs and above) 2 doses - Ad5-nCoV-placebo

EBOV A: n=34 IM, 2 doses - Ad5-nCoV

EBOV B: n=17 IM, 2 doses - Ad5-nCoV-placebo

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

VII. VACCINE NAME: HAD5-S-FUSION+N-ETSD

MANUFACTURER: ImmunityBio, Inc.

VACCINE PLATFORM: Human adenovirus serotype 5 (hAd5) vector with E1/E2b/E3 deletions expressing SARS-CoV-2 viral antigen spike fusion protein and nucleocapsid with an enhanced T-cell stimulation domain. The elimination of E1-E3 genes from Ad5 leads to a decrease in anti-vector immunity.

TRIAL REGISTRATION #: NCT04591717

AVAILABILITY: Not available. Phase I study started on 19th October 2020, proposed study completion date, 19th November 2020.

BRIEF SUMMARY:

Non-randomized study (n=35), 18 – 55 years old, divided into 3 groups: 5 x 10^{10} VP (n=10), 1 x 10^{11} VP (n=10) and either 5 x 10^{10} or 1 x 10^{11} VP (n=15). Both genders to be accepted.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

VIII. VACCINE NAME: MVA-SARS-2-S

MANUFACTURER: Universitätsklinikum Hamburg-Eppendorf (University Medical Centre of Hamburg-Eppendorf) collaborating with German Centre for Infection Research, Phillipps University Marburg Medical Centre and Ludwig-Maximillians – University of Munich.

VACCINE PLATFORM: Modified Vaccinia Virus Ankara (MVA) vector expressing the SARS-CoV-2 spike protein.

TRIAL REGISTRATION #: NCT04569383

AVAILABILITY: Not available. Phase I study started on 5th October 2020, proposed study completion date May 2021.

BRIEF SUMMARY:

A non-randomized study with 30 participants assessing the effects, safety, tolerability and immunogenicity of two ascending doses of the vaccine.

Two cohorts – 1 x 10^{7} infectious units and 1x 10^{8} infectious units. Vaccinations to occur at day 0 and day 28.

18 – 55 years, males and females. Patients with hypersensitivities or previous rMVA immunisation excluded.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

IX. VACCINE NAME: COVISHIELD (SII-CHADOX1 NCOV-19)

MANUFACTURER: Serum Institute of India Private Ltd/ India Council of Medical Research with technical collaboration from Oxford University/Astra Zeneca

VACCINE PLATFORM: A replication-deficient simian adenovirus vector ChAdOx1, containing the structural surface glycoprotein (Spike protein) antigens of SARS-CoV-2.

TRIAL REGISTRATION #: CTRI/2020/08/027170,

AVAILABILITY: Not available. Phase 2/3 study started on 24th August 2020, no information on completion date.

BRIEF SUMMARY:

Randomized, observer-blind study in 1600 Indian participants, 18 – 99 years old. Safety and immunogenicity of COVISHEILD to be compared with Oxford/AZ-ChAdOx1 nCoV-19 and placebo.

Immunogenicity cohort: 400 participants – 3:1 ratio receiving COVISHEILD or Oxford/AZ-ChAdOx1 nCoV-19 respectively.

Safety Cohort: 1200 participants - 3:1 ratio receiving COVISHEILD or placebo respectively

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

SUMMARY STATEMENT:

It is noted that a volunteer alleged that the vaccine caused severe adverse effects including neurological breakdown and impaired cognitive functions. It will be important to pay particular attention to safety data and compare it to its counterpart from the Oxford/AstraZeneca data.

X. VACCINE NAME: AD26.COV2.S

MANUFACTURER: Janssen Vaccines & Prevention B.V.

VACCINE PLATFORM: a human replication-incompetent Ad26 vector, constructed to encode the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus spike (S) protein.

TRIAL REGISTRATION #: NCT04505722, NCT04614948,

AVAILABILITY: Not available. Phase 3 study started 7th September and 15th November 2020, proposed study completion date, 10th March - 11th May 2023.

BRIEF SUMMARY:

Randomized, double-blind, placebo-controlled studies to assess the efficacy and safety of Ad26.COV2.S for the prevention of SARS-COV-2-mediated COVID-19 in adults aged 18 years and older. Study participants would include those with stable co-morbidities, as they are part of the at-risk group for Covid-19, information on their response to experimental vaccines is needed.

NCT04614948

To include 30,000 participants in Belgium, Colombia, France, Germany, Philippines, South Africa, Spain, United Kingdom, US will participate in a screening phase (up to 28 days), double-blind study period (60-week), and a long-term follow-up period (1 additional year). The total study duration will be maximum 2 years and 3 months. Assessments would include efficacy (COVID-19-like signs and symptoms, etc), immunogenicity (humoral immune responses) and safety (AEs monitoring) and will be performed throughout the study. Participants will receive intramuscular injection of Ad26.COV2.S vaccine or placebo on Day 1 and Day 57.

NCT04505722

To include 60,000 participants from Argentina, Brazil, Chile, Colombia, Mexico, Peru, Philippines, South Africa, Ukraine, United States of America will participate in this study. Participants will receive intramuscular (IM) injection of Ad26.COV2.S vaccine at a dose level of $5x10^{10}$ virus particles (vp) as single dose vaccine or placebo on Day 1.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: NOT KNOWN.

XI. VACCINE NAME: SPUTNIK V/GAM-COVID-VAC

MANUFACTURER: Gamaleya Research Institute

VACCINE PLATFORM: non-replicating recombinant human adenovirus vectors (DNA), both carrying the gene for the SARS-CoV-2 full length glycoprotein S: adenovirus type 26 (rAd26-S) and adenovirus type 5 (rAd5-S) vectors.

AVAILABILITY: Not available. Phase 2 study started on 22nd October 2020, proposed study completion date, 31st December 2021.

BRIEF SUMMARY:

A non-randomized trial in 110 participants, 60 – 111 years old, given 0.5 mL/dose + 0.5 mL dose prime boost on day 1 –rAd26-S and day 21 – rAd5-S. All genders to be included. This study is occurring in Russia. Of note, the lyopholised version is not being tested.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: NOT KNOWN.

6.1.2 Replicating Viral Vector Vaccines (Recruiting)

These vaccines are based on a modified virus (the vector) to deliver genetic code for the antigen. By infecting cells and instructing them to make large amounts of antigen, which then triggers an immune response. The replicating vector vaccine also produces new viral particles in the cells they infect, which then go on to infect new cell that will also make the vaccine antigen (as opposed to non-replicating vector vaccines which are unable to produce new viral particles, they only produce vaccine antigen).

I. VACCINE NAME: DELNS1-2019-NCOV-RBD-OPT1

MANUFACTURER: Beijing Wantai Biological Pharmacy/ Xiamen University

AVAILABILITY: Not available. Phase 1 approved 31/8/2020; Phase 2 approved 29/10/2020

BRIEF SUMMARY:

A Phase I Clinical Trial of Influenza virus Vector COVID-19 Vaccine for intranasal Spray ChiCTR2000037782. Number of doses: 1

A Phase II Clinical Trial of Influenza virus Vector COVID-19 Vaccine for intranasal Spray (DelNS1-2019-nCoV-RBD-OPT1). ChiCTR2000039715. Number of doses: 1.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: NOT KNOWN.

STUDY STATUS: RECRUITING.

II. VACCINE NAME: IIBR-100

MANUFACTURER: Israel Institute for Biological Research

AVAILABILITY: Not available.

BRIEF SUMMARY:

A Phase I/II Randomized, Multi-Center, Placebo-Controlled, Dose-Escalation Study to Evaluate the Safety, Immunogenicity and Potential Efficacy of an rVSV-SARS-CoV-2-S Vaccine (IIBR-100) in Adults. NCT04608305

Two phases, a dose escalation phase I and expansion to phase II that includes larger cohorts

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: NOT KNOWN.

STUDY STATUS: RECRUITING.

III. VACCINE NAME: COH04S1

MANUFACTURER: City of Hope, USA (NCT04639466)

AVAILABILITY: Not available.

BRIEF SUMMARY: Phase 1 Dose Escalation Study to Evaluate the Safety and Biologically Effective Dose of COH04S1, a Synthetic MVA-Based SARS-CoV-2 Vaccine, Administered as One or Two Injections to Healthy Adult Volunteers.

Phase 1 study – dose escalation study, participants are randomized to 1 of 3 arms and receive vaccine on day 0 and day 28: 2 doses of vaccine, single dose of vaccine and then placebo or 2 doses of placebo.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: NOT KNOWN.

STUDY STATUS: RECRUITING.

IV. VACCINE NAME: V590

MANUFACTURER: Merck Sharp & Dohme/IAVI (NCT04569786)

AVAILABILITY: Not available.

BRIEF SUMMARY: A Phase 1, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Trial to Evaluate the Safety and Immunogenicity of V590 in Healthy Adults. Number of doses: 1

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: NOT KNOWN.

STUDY STATUS: RECRUITING.

V. VACCINE NAME: MEASLES VECTOR-BASED VACCINE CANDIDATE

MANUFACTURER: Institute Pasteur/Themis/Univ. of Pittsburg CVR/Merck Sharp & Dohme

BRIEF SUMMARY: A Randomized, Placebo-controlled Trial, to Evaluate the Safety and Immunogenicity of the COVID-19 Vaccine, a Measles Vector-based Vaccine Candidate Against COVID-19 in Healthy Volunteers Consisting of an Unblinded Dose Escalation and a Blinded Treatment Phase. [NCT04497298]. Number of doses: 1 or 2 doses, 28 days apart.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: NOT KNOWN.

STUDY STATUS: RECRUITING.

6.1.3 DNA Vaccines

DNA vaccines entail introducing into appropriate tissues, a plasmid containing the DNA sequence encoding the antigen against which an immune response is sought.

This method relies on the in-situ production of the target antigen. Advantages of DNA vaccines include the stimulation of both B and T cell responses and the absence of infectious agents.

There are currently no DNA vaccines available against COVID-19. Of note, in mid-2019, Phase one trial results were released for a vaccine against Middle East Respiratory Syndrome, a disease which emerged in 2012. The results supported the continuation of the trial.

There are currently no DNA vaccines against COVID-19 available on the market. Six candidate vaccines are in development at various stages in Phase 1 and 2 studies.

BRIEF SUMMARIES OF STUDIES:

1. Inovio Pharmaceuticals/ International Vaccine Institute
   DNA plasmid vaccine with electroporation. 2 doses at 0, 28 days administered intradermally.

   NCT04447781 NCT04336410 NCT04642638 ChiCTR2000040146. Phase 1 and Phase 2 stages with no results.

   NCT04447781 – study completion Feb 2022; NCT04336410 – study completion July 2021; NCT04642638 – study completion September 2022.

2. Osaka University/ AnGes/ Takara Bio DNA plasmid vaccine + Adjuvant; 2 doses at 0, 14 days given intramuscularly. Phase 1, 2 - no results. NCT04463472 - Study completion July 2021. NCT04527081 - Study completion September 2021.

3. Cadila Healthcare Limited DNA plasmid vaccine 3 doses at 0, 28, 56 days. ID CTRI/2020/07/026352.

4. Genexine Consortium DNA Vaccine (GX-19) 2doses at 0, 28 days IM. NCT04445389 – recruiting; study end date June 2022.

5. Symvivo DNA bacTRL-Spike. 1dose Oral. NCT04334980 – recruiting; study end date February 2022.

6. Providence Health & Services DNA electroporated S protein plasmid DNA vaccine with or without the combination of electroporated IL12p70 plasmid. Two doses at 0, 28 days ID NCT04627675 – not yet recruiting; study end date May 2022

OVERALL QUALITY OF EVIDENCE: Not known.

SUMMARY STATEMENT:

It is too early to make a recommendation on DNA vaccines for COVID-19. However, Phase 1 results should be available from 2021 for some of the trials.

6.1.4 Inactivated Vaccines

The new technologies used in the development of vaccines from major pharmaceutical firms utilize newer methodologies that can manufacture vaccines quickly and a makes mass production more efficient. Inactivated vaccines are centered around technologies that have been utilized for decades. It comprises virus particles that has been inactivated by heat, chemical or radiation such that it hinders their ability to replicate but can still illicit an immune response. Inactivated vaccines boast a high safety and efficacy profile with billions of persons being vaccinated using this technology over the last century. Inactivated vaccines are generally more stable during long-term storage and are typically developed as liquid formulations stored in glass vials and prefilled syringes.

I. VACCINE NAME: CORONAVAC – PHASE I AND II

MANUFACTURER: Sinovac Life Sciences (Beijing, China), Sinovac Biotech Co., Ltd (Sinovac Research and Development Co., Ltd.)

VACCINE PLATFORM: CoronaVac is an inactivated vaccine candidate created from African green monkey kidney cells (Vero cells) inoculated with SARS-CoV-2 (CN02 strain). After incubation the virus was harvested and inactivated with β-propiolactone. It was then concentrated, purified, and

absorbed onto aluminium hydroxide. The aluminium hydroxide complex was then diluted in a sodium chloride, phosphate-buffered saline, and water solution before being sterilised and filtered ready for injection. The placebo is aluminium hydroxide diluent solution with no virus.

AVAILABILITY: Approved of emergency use in China. Currently in Phase 3 studies.

BRIEF SUMMARY:

Randomized, double-blind, placebo-controlled, phase 1/2 clinical trial. Participants given either low dose [3 µg/ 0·5 mL Al(OH)3 diluent] or high dose [6 µg/0·5 mL Al(OH)3 diluente]. Participant received two doses of vaccine or placebo on day 0 and 14 or day 0 and 28.

OUTCOMES:

PHASE *1 trial (n=144)*

INCIDENCE OF ADVERSE EVENTS:

3 ug group: 7/24 (29%); 6 µg group: 9/24 (38%); Placebo group: 2/24 (8%)

SEROCONVERSION OF NEUTRALIZING ANTIBODIES:

At day 14, after the days 0 and 14 vaccination schedule - 3 µg group: 11/24 (46%); 6 µg group: 12/24 (50%); Placebo group: 0/24 (0%).

At day 28, after days 0 and 28 vaccination schedule - 3 µg group: 20/24 (83%); 6 µg group: 19/24 (79%); Placebo group: 1/24 (4%).

PHASE 2 TRIAL (N=600)

INCIDENCE OF ADVERSE REACTIONS:

(0- and 14-day cohort) - 3 µg group: 40/120 (33%); 6 µg group: 42/120 (35%); Placebo group: 13/60 (22%)

(0- and 28-day cohort) - 3 µg group: 23/120 (19%); 6 µg group: 23/120 (19%); Placebo group: 11/60 (18%)

SEROCONVERSION OF NEUTRALIZING ANTIBODIES:

At day 14, 0 - 14 days trial - 3 µg group: 109/118 (92%); 6 µg group: 117/119 (98%); Placebo group: 2/60 (3%).

At day 28, 0 and 28 day trial - 3 µg group: 114/117 (97%); 6 µg group: 118/118 (100%); Placebo group: 0/59 (0%)

SAFETY: The most common adverse effect reported in the Phase I and II trials were pain and swelling at injection site. Safety endpoint: adverse reactions within 28 days.

IMMUNOGENIC OUTCOME: seroconversion rates of neutralizing antibodies to live SARS-CoV-2 at day 14 after the last dose in the days 0 and 14 cohort, and at day 28 after the last dose in the days 0 and 28 cohort.

OVERALL QUALITY OF EVIDENCE: LEVEL III/HIGH GRADE/ LOW RISK OF BIAS

SUMMARY STATEMENT:

This study was conducted only in Asians (possibly Chinese). Approved for emergency use in China whilst undergoing Phase 3 trials. The vaccine efficacy remains to be determined.

STATUS: Phase I/II trials completed; Phase III is ongoing.

II. VACCINE NAME: BBV152 (PHASE I/II)

MANUFACTURER: Bharat Biotech

VACCINE PLATFORM: BBV152 is a whole-virion, inactivated SARS-CoV-2 vaccine. The candidates were formulated with two adjuvants: Algel (alum) and Algel-IMDG, an imidazoquinoline class molecule (IMDG) adsorbed onto Algel. Three vaccine formulations were prepared as follows: 3 µg with Algel-IMDG, 6 µg with Algel- IMDG and 6 µg with Algel. The placebo group contained only a sterile phosphate buffered solution and Algel. The vaccine was provided as a sterile liquid for intramuscular injection (0.5 mL/dose) in a two-dose regimen with a 14-day interval. Both vaccine and control were stored between 2°C and 8°C.

AVAILABILITY: Not available.

BRIEF SUMMARY:

A Randomized, parallel-group, active controlled trial using whole-virion inactivated SARS-CoV-2 Vaccine (BBV152) in healthy volunteers. This study was an adaptive, seamless Phase 1, followed by Phase 2 randomized, double-blind, multicenter study to evaluate the safety, reactogenicity, tolerability and immunogenicity of the whole-virion inactivated SARS-CoV-2 Vaccine (BBV152) in healthy volunteers.

A vaccine/placebo was administered on day 0 and Day 14. Follow-up visits were scheduled on days 7, 28, 42, 104, and 194.

OUTCOME MEASUREMENTS

- *Immunogenicity* - Neutralizing Antibody Titers
- *Safety* – local and systemic adverse reactions

OUTCOMES

IMMUNOGENICITY

Neutralizing Antibody Titers - The proportions of participants with seroconversion (after 2nd dose) were 87.9%, 91.9%, 82.8% in the 3 µg with Algel-IMDG, 6 µg with Algel-IMDG, and 6 µg with Algel groups, respectively. Seroconversion (at day 28) in control arm was 6 (8%) participants, suggestive of a high degree of ongoing infection. The post 2nd dose GMTs in the three vaccine arms were 61.7, 66.4, and 48.0 in the 3 µg with Algel-IMDG, 6 µg with Algel-IMDG and 6 µg with Algel groups, respectively.

SAFETY

After 1st vaccination, local and systemic adverse events were mostly mild or moderate, resolved rapidly without any prescribed medication. A similar trend was observed after 2nd vaccination. Pain at injection site was the most common local adverse event in the Algel-IMDG groups. The distribution of local and systemic AEs was equal among vaccination and control groups.

OVERALL QUALITY OF EVIDENCE: Level III/High Grade/ Low risk of bias

SUMMARY STATEMENT:

BBV152 induced binding and neutralizing antibody responses and with the inclusion of the Algel-IMDG adjuvant, this is the first inactivated SARS-CoV-2 vaccine that has been reported to induce a Th1-biased response. BBV152 is stored between 2°C and 8°C, which is compatible with all national immunization programs. Both Algel-IMDG formulations were selected for the Phase 2 immunogenicity trials. Further Phase 3 efficacy trials are underway.

STATUS: Phase I/II trials completed. Phase III is ongoing.

III. VACCINE NAME: WIV04 STRAIN (PHASE I AND II TRIAL).

MANUFACTURER: Wuhan Institute of Biological Products Co Ltd.

VACCINE PLATFORM: A SARS-CoV-2 strain was isolated from a patient in Wuhan and cultivated in a qualified Vero cell line for propagation. The supernatant was inactivated with β-propiolactone (1:4000 vol/vol) at 2 to 8 °C for 48 hours. Following clarification and ultrafiltration, the second β-propiolactone inactivation was performed under similar conditions. The vaccine was adsorbed to 0.5-mg alum and packed into prefilled syringes in 0.5-mL sterile phosphate-buffered saline without preservative. Placebo contained sterile phosphate-buffered saline and alum adjuvant.

AVAILABILITY: Not available.

BRIEF SUMMARY:

Double-blind, randomized, placebo-controlled phase 1 & 2 trials with 750 Chinese participants.

PHASE 1 trial: 96 participants received 3 vaccine dose groups (low, medium, and high doses with 2.5-, 5-, 10-µg antigen protein per dose). Intramuscular injections on days 0, 28, and 56.

Phase 2 trial: 224 participants received 2 schedule groups (days 0 and 14, and days 0 and 21) using the medium (5-µg) dose.

OUTCOMES:

HUMORAL IMMUNOGENICITY

Seroconversion was noted in all participants (100%) receiving vaccines in the low- and high-dose groups in phase 1, 23 of 24 participants (95.8%) in the medium-dose group in phase 1, and 41 of 42 participants (97.6%) in the 2 groups in phase 2, but none in the alum-only group.

SAFETY

The most common adverse reaction was injection site pain (14 in phase 1 and 21 in phase 2), followed by fever (2 in phase 1 and 8 in phase 2). All adverse reactions were mild (grade 1 or 2), transient, and self-limiting, and did not require any treatment.

PRIMARY SAFETY OUTCOME IN BOTH PHASES:

Injection site–specific adverse reactions (pain, redness, and swelling) and systemic adverse reactions (fever, headache, and fatigue) on diary cards within 7 days of each injection).

OVERALL QUALITY OF EVIDENCE: Level III/High Grade/ Low risk of bias

SUMMARY STATEMENT:

This represents a phase I/II trial and shows good seroconversion rates with low incidence of adverse effects. Phase 3 studies are required to determine vaccine efficacy and long term safety.

STATUS: Phase I/II completed.

IV. VACCINE NAME: VLA2001 (PHASE I AND II)

MANUFACTURER: Valneva (FRANCE)

VACCINE PLATFORM: VLA2001 has inactivated whole virus particles of SARS-CoV-2 with high S-protein density and two adjuvants, alum and CpG 1018.

VLA2001 is the first inactivated vaccine for Covid-19 to initiate clinical development in Europe and leverages the manufacturing platform of the firm's licensed Japanese encephalitis vaccine, IXIARO.

AVAILABILITY: Not available, started on 16th July 2020, proposed completion date 15th July 2021.

BRIEF SUMMARY: The randomized, double-blind and placebo-controlled trial will analyze the safety and immunogenicity of the vaccine at three dose levels three weeks apart in around 150 healthy adults.

Initially, the study will begin with an open-label dose-escalation phase and the participants will receive intramuscular doses of the vaccine.

OUTCOME MEASUREMENTS

The primary endpoint read-out will be two weeks following the conclusion of the two-dose primary immunization given on days 0 and 21.

SAFETY

Unknown

OVERALL QUALITY OF EVIDENCE: Not known.

V. VACCINE NAME: BBIBP-CORV– PHASE III TRIAL

MANUFACTURER: Beijing Institute of Biological Products/Sinopharm

VACCINE PLATFORM: Three isolated SARS-CoV-2 strains [19nCoV-CDC-Tan-HB02 (HB02), 19nCoV-CDC-Tan-Strain03 (CQ01), and 19nCoV-CDC-Tan-Strain04 (QD01)] were used to develop preclinical *in vitro* neutralization and challenge models for an inactivated SARS-CoV-2 vaccine candidate. The three strains were Vero cells, but not other cell lines, were infected via the throat swabs of patients to prevent possible mutations during viral culture and isolation.

HB02 strain showed the most optimal replication and generated highest virus yields in Vero cells among three viral strains and was therefore used for the development of the inactivated SARS-CoV-2 vaccine (BBIBP-CorV).

To inactivate virus production, β-propionolactone was thoroughly mixed with the harvested viral solution at a ratio of 1:4,000 at 2-8°C. The inactivation of three batches of virus eliminated viral infectivity, validating the good stability, and repeatability of the inactivation process. Western blot analysis showed that the vaccine stock contained viral structural proteins (protective antigens). A negatively stained electron microscopy image visualized oval viral particles with spikes with the diameters of approximately 100nm.

AVAILABILITY: Not available, started on 16th July 2020, proposed completion date 15th July 2021.

BRIEF SUMMARY: A Phase 3 clinical trial for inactivated novel coronavirus pneumonia (COVID-19) vaccine (Vero cells). A randomized, double blind, parallel placebo controlled, Phase 3 Clinical Trial to evaluate the safety and protective efficacy of inactivated SARS-CoV-2 Vaccine in a healthy Chinese population aged 18 years and above.

Inclusion criteria:

1. Healthy subjects aged 18 years old and above in good health.

2. Female subjects of childbearing age are not nursing or pregnant at the time of enrolment (negative urine pregnancy test) and have no family planning within the first 3 months after enrolment. Effective contraceptive measures have been taken within 2 weeks before inclusion.

3. During the whole follow-up period of the study, be able and willing to complete the whole prescribed study plan. With self-ability to understand the research procedures, the informed consent & voluntarily sign an informed consent form and be able to comply with the requirements of the clinical study protocol.

EXCLUSION CRITERIA:

1. SARS-CoV-2 Infection Confirmed Cases, Suspected Cases or Asymptomatic Infection.

2. SARS-CoV-2 Nucleic acid test positive.

3. Have a history of SARS, MERS infection (self-report, on-site inquiry).

4. Fever (axillary temperature > 37.0 degree C), dry cough, fatigue, nasal obstruction, runny nose, pharyngeal pain, myalgia, diarrhea, shortness of breath and dyspnea occurred within 14 days before vaccination.

5. Axillary body temperature >37.0 degree C before vaccination.

6. Previous severe allergic reactions to vaccination (such as acute allergic reactions, urticaria, dyspnea, angioneurotic edema or abdominal pain) or allergy to known ingredients of inactivated SARS-CoV-2 vaccine have occurred.

7. Have a history of convulsion, epilepsy, encephalopathy or mental illness or family history.

8. Congenital malformations or developmental disorders, genetic defects, severe malnutrition.

OUTCOME MEASUREMENTS

Vaccine efficacy

To evaluate the protective effect 14 days after 2 doses of immunization of preventing severe cases of SARS-CoV-2 pneumonia and deaths accompanied by COVID-19.

Safety

Incidence of adverse reactions/events, serious adverse events (SAE)

Measure time point of outcome: Within 12 months from first vaccination to completion of full vaccination schedule.

OVERALL QUALITY OF EVIDENCE: Not known.

VI. VACCINE NAME: BBV152 - PHASE III TRIAL

MANUFACTURER: Bharat Biotech

VACCINE PLATFORM:

BBV152 is a whole-virion, inactivated SARS-CoV-2 vaccine. The candidates were formulated with two adjuvants: Algel (alum) and Algel-IMDG, an imidazoquinoline class molecule (IMDG) adsorbed onto Algel. Three vaccine formulations were prepared as follows: 3 µg with Algel-IMDG, 6 µg with Algel- IMDG and 6 µg with Algel. The placebo group contained only a sterile phosphate buffered solution and Algel. The vaccine was provided as a sterile liquid for intramuscular injection (0.5 mL/dose) in a two-dose regimen with a 14-day interval. Both vaccine and control were stored between 2°C and 8°C.

AVAILABILITY: Not currently available. Study started on 25th November 2020 in India, estimated study completion date 1st March 2022.

BRIEF SUMMARY:

A Phase III, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy, safety, immunogenicity, and Lot-to-Lot consistency of BBV152, a Whole virion inactivated vaccine in adults greater than or equal to 18 Years of Age.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

VII. VACCINE NAME: CORONAVAC- PHASE III

MANUFACTURER: PT. Bio Farma, Sinovac Life Sciences

VACCINE PLATFORM: CoronaVac is an inactivated vaccine candidate against COVID-19, created from African green monkey kidney cells (Vero cells) that have been inoculated with SARS-CoV-2 (CN02 strain). Once the incubation period was over, the virus was harvested and inactivated with β-propiolactone. It was then concentrated, purified, and absorbed onto aluminium hydroxide. The aluminium hydroxide complex was then diluted in a sodium chloride, phosphate-buffered saline, and water solution before being sterilized and filtered ready for injection. The placebo is aluminium hydroxide diluent solution with no virus.

AVAILABILITY: Not available. Completion date is 15th April 2021**.**

BRIEF SUMMARY:

A Phase III, Observer-blind, Randomized, Placebo-controlled Study of the Efficacy, Safety and Immunogenicity of SARS-CoV-2 Inactivated Vaccine in Healthy Adults Aged 18-59 Years in Indonesia. Two doses at 14-day interval, each inoculation dose is 0.5 mL. Two doses of dosage (each prefilled syringe of the vaccine contains 600 SU of SARS-CoV-2 virus antigen) experimental vaccine at the schedule of day 0, 14. Placebo is aluminium hydroxide, disodium hydrogen phosphate, sodium dihydrogen phosphate, sodium chloride 0.5mL/dose, two doses given 14 days apart.

Inclusion Criteria:

1. Clinically healthy adults aged 18 – 59 years.

2. Negative IgG and IgM for SARS-CoV-2 (by standardize rapid test).

3. Subjects have been informed properly regarding the study and signed the informed consent form.

4. Subjects will commit to comply with the instructions of the investigator and the schedule of the trial.

Exclusion Criteria:

1. Subjects concomitantly enrolled or scheduled to be enrolled in another trial.

2. Contact with novel coronavirus infected persons (positive for nucleic acid detection) within 14 days prior to the trial.

3. Contact to patients with fever or respiratory symptoms surrounding areas or from communities with reported cases within 14 days prior to the trial.

4. Two or more cases of fever and/or respiratory symptoms in a small area such as home, office, school and class within 14 days prior to the trial.

5. Evolving mild, moderate or severe illness, especially infectious disease or fever (body temperature ≥37.5℃, measured with infrared thermometer/thermal gun).

6. Women who are lactating, pregnant or planning to become pregnant during the study period (judged by self-report of subjects and urine pregnancy test results).

7. History of asthma, history of allergy to vaccines or vaccine ingredients, and severe adverse reactions to vaccines, such as urticaria, dyspnea, and angioneurotic edema.

8. History of uncontrolled coagulopathy or blood disorders contraindicating intramuscular injection.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

VIII. VACCINE NAME: WIV04 STRAIN - PHASE III TRIAL

MANUFACTURER: Wuhan Institute of Biological Products Co Ltd

VACCINE PLATFORM: A SARS-CoV-2 strain (National Genomic Data Center of the Chinese Academy of Science accession No. SAMC133237, and GenBank accession number MN996528) was isolated from a patient in the Jinyintan Hospital, Wuhan. The virus was cultivated in a qualified Vero cell line for propagation, and the supernatant of the infected cells was inactivated with β-propiolactone (1:4000 vol/vol at 2 to 8 °C for 48 hours. Following clarification of cell debris and ultrafiltration, the second β-propiolactone inactivation was performed in the same conditions as the first inactivation. The vaccine was adsorbed to 0.5-mg alum and packed into prefilled syringes in 0.5-mL sterile phosphate-buffered saline without preservative. The placebo group contained only sterile phosphate-buffered saline and alum adjuvant.

AVAILABILITY: Not available.

BRIEF SUMMARY:

Randomized, double-blinded, placebo parallel-controlled phase III clinical trial to evaluate the Immunogenicity and safety of the inactivated SARS-CoV-2 Vaccine (Vero cell) in healthy population aged 18 years and above. Placebo is aluminum hydroxide (alum) adjuvant only.

OUTCOME MEASUREMENTS:

To evaluate the 4-fold increase rate, GMT and GMI of anti-SARS-CoV-2 neutralizing antibody 28 days after full course of immunization:

- 28 days after the full course of vaccination: incidence of adverse reactions/events
- Within 30 minutes after each dose of vaccination: incidence of adverse reactions/events
- Within 0-7 and 8-21/28 days after each dose of vaccination: Serious Adverse Events
- Within 12 months from first vaccination to completion of full vaccination schedule: Protective efficacy against COVID 19

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

6.1.5 Protein Subunit Vaccines

Subunit vaccines do not contain live viral components and are considered very safe. These vaccines comprise of only the components or antigens of the pathogen that best stimulate the immune system, i.e., they contain the antigenic parts of the pathogen which are necessary to elicit a protective immune response and would also minimize side effects. This design strategy which requires precision, can make vaccines safer and easier to produce, but requires the inclusion of adjuvants to stimulate a strong protective immune response because antigens alone are not sufficient to induce long-term immunity.

I. VACCINE NAME: SARS-COV-2 RS NANOPARTICLE VACCINE (NVX-COV2373)

MANUFACTURER: **Novavax**

AVAILABILITY: Not available. Trials started on 25th May 2020, primary completion date 1st December, study completion date 18th November 2021. [NCT04368988].

VACCINE PLATFORM: Protein Subunit / Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M.

BRIEF SUMMARY:

A 2-Part, Phase 1/2, Randomized, Observer-Blinded Study to Evaluate the Safety and Immunogenicity of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) With or Without MATRIX-M™ Adjuvant in Healthy Subjects.

Part 1 (Phase 1) of the study is designed to evaluate the safety and immunogenicity of SARS-CoV-2 rS nanoparticle vaccine with or without Matrix-M adjuvant in 131 healthy participants ≥ 18 to 59 (inclusive) years of age at 2 sites in Australia.

Part 2 (Phase 2) of the study is designed to evaluate the immunogenicity, safety, and preliminary efficacy of a single construct of SARS-CoV-2 rS nanoparticle vaccine with Matrix-M adjuvant in up to 1,500 healthy participants ≥ 18 to 84 (inclusive) years of age at up to 40 sites across Australia and/or the United States.

ARMS: Ten treatment groups

- Placebo Comparator: Placebo - Phase 1 (2 doses of Placebo (Saline), 1 dose each on Days 0 and 21); Intervention: Other: Normal saline solution (NSS), Placebo.

- Experimental: SARS-CoV-2 rS - 25µg without Matrix-M - Phase 1 (2 doses of SARS-CoV-2 rS - 25µg, 1 dose each on Days 0 and 21. Intervention: Biological: SARS-CoV-2 rS - Phase 1
- Experimental: SARS-CoV-2 rS - 5µg + 50µg Matrix-M - Phase 1(2 doses of SARS-CoV-2 rS - 5µg + 50µg Matrix-M (mixed together for each injection), 1 dose each on Days 0 and 21. Intervention: Biological: SARS-CoV-2 rS/Matrix-M Adjuvant - Phase 1
- Experimental: SARS-CoV-2 rS - 25µg + 50µg Matrix-M - Phase 1(2 doses of SARS-CoV-2 rS - 25µg + 50µg Matrix-M (mixed together for each injection), 1 dose each on Days 0 and 21. Intervention: Biological: SARS-CoV-2 rS/Matrix-M Adjuvant - Phase 1
- Experimental: SARS-CoV-2 rS - 25µg + 50µg Matrix-M then Placebo - Phase 1 (1 dose of SARS-CoV-2 rS - 25µg + 50µg Matrix-M (mixed together for injection), on Day 0 followed by 1 dose of Placebo on Day 21. Interventions:
    - Biological: SARS-CoV-2 rS/Matrix-M Adjuvant, Day 0 - Phase 1
    - Other: Normal saline solution (NSS), Placebo, Day 21 - Phase 1
- Placebo Comparator: Placebo - Phase 2 (3 doses of Placebo (Saline), 1 dose each on Days 0, 21, and 189. Intervention: Other: Normal saline solution (NSS), Placebo - Phase 2
- Experimental: SARS-CoV-2 rS - 5/5µg + 50µg Matrix-M - Phase 2 (2 doses of SARS-CoV-2 rS - 5 µg + 50 µg Matrix-M (co-formulated), 1 dose each on Days 0 and 21, followed by 1 dose of Placebo on Day 189. Interventions:
    - Biological: SARS-CoV-2 rS/Matrix-M Adjuvant, Days 0 and 21 - Phase 2
    - Other: Normal saline solution (NSS), Placebo, Day 189 - Phase 2
- Experimental: SARS-CoV-2 rS - Alternating 5µg + 50µg Matrix-M - Phase 2 (1 dose of SARS-CoV-2 rS - 5µg + 50µg Matrix-M (co-formulated) on Day 0 then 1 dose of Placebo on Day 21 followed by 1 dose of SARS-CoV-2 rS - 5µg + 50µg Matrix-M (co-formulated) on Day 189. Interventions:
    - Biological: SARS-CoV-2 rS/Matrix-M Adjuvant, Day 0 - Phase 2
    - Other: Normal saline solution (NSS), Placebo, Day 21 - Phase 2
    - Biological: SARS-CoV-2 rS/Matrix-M Adjuvant - Day 189 - Phase 2
- Experimental: SARS-CoV-2 rS - 25/25µg + 50µg Matrix-M - Phase 2 (2 doses of SARS-CoV-2 rS - 25µg + 50µg Matrix-M (co-formulated), 1 dose each on Days 0 and 21, followed by 1 dose of Placebo on Day 189. Interventions:
    - Biological: SARS-CoV-2 rS/Matrix-M Adjuvant, Days 0 and 21 - Phase 2
    - Other: Normal saline solution (NSS), Placebo, Day 189 - Phase 2

- Experimental: SARS-CoV-2 rS - Alternating 25/5µg + 50 µg Matrix-M - Phase 2 (1 dose of SARS-CoV-2 rS - 25µg + 50µg Matrix-M (co-formulated) on Day 0 then 1 dose of Placebo on Day 21 followed by 1 dose of SARS-CoV-2 rS - 5µg + 50 µg Matrix-M (co-formulated) on Day 189. Interventions:
    - Biological: SARS-CoV-2 rS/Matrix-M Adjuvant, Day 0 - Phase 2
    - Other: Normal saline solution (NSS), Placebo, Day 21 - Phase 2
    - Biological: SARS-CoV-2 rS/Matrix-M Adjuvant - Day 189 - Phase 2

SAFETY: Two-dose regimens of 5µg and 25µg of rSARS-CoV-2 plus the Matrix-M1 adjuvant had acceptable safety findings and induced high immune responses.

OVERALL QUALITY OF EVIDENCE: Level III/High Grade/High risk of bias. Results from Phase 1 studies. The adjuvanted, recombinant, full-length spike protein nanoparticle vaccine NVX-CoV2373 is a promising candidate that warrants testing in efficacy studies.

STATUS: Phase 2 trials **o**ngoing and Phase 3 trial in preparatory stages.

II. VACCINE NAME: RECOMBINANT SARS COV-2 GLYCOPROTEIN NANOPARTICLE (SARS-COV-2 RS)

MANUFACTURER: Novavax

AVAILABILITY: Not available. Phase 1/2 study started on 17th August 2020, completion date November 2021. [NCT04533399]

VACCINE PLATFORM: Protein Subunit/Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix.

BRIEF SUMMARY:

A Phase 2A/B, Randomized, Observer-blinded, Placebo-controlled Study to Evaluate the Efficacy, Immunogenicity, and Safety of a **SARS-CoV-2** Recombinant Spike Protein Nanoparticle **Vaccine** (**SARS-CoV-2** rS) With Matrix-M1™ Adjuvant in South African Adult Subjects Living Without HIV; and Safety and Immunogenicity in Adults Living With HIV.

Four treatment groups

- Experimental: Cohort 1 (HIV negative) 5 µg SARS-CoV-2 rS/Matrix-M1 Adjuvant (2 doses of SARS-CoV-2 rS - 5 µg + 50 µg Matrix-M1 adjuvant (co-formulated), 1 dose

each on Days 0 and 21). Intervention: Biological: SARS-CoV-2 rS/Matrix-M1 Adjuvant

- Placebo Comparator: Cohort 1 (HIV negative) Placebo (2 doses of Placebo, saline), 1 dose each on Days 0 and 21. Intervention: Other: Placebo.
- Experimental: Cohort 2 (HIV positive) 5 µg SARS-CoV-2 rS/Matrix-M1 Adjuvant (2 doses of SARS-CoV-2 rS - 5 µg + 50 µg Matrix-M1 adjuvant (co-formulated), 1 dose each on Days 0 and 21. Intervention: Biological: SARS-CoV-2 rS/Matrix-M1 Adjuvant.
- Placebo Comparator: Cohort 2 (HIV positive) Placebo. 2 doses of Placebo (Saline), 1 dose each on Days 0 and 21. Intervention: Other: Placebo

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Phase 1/2/Recruiting

III. VACCINE NAME: SARS-COV-2 RS

MANUFACTURER: Novavax

AVAILABILITY: Not available. Phase 3 to start December 2020, completion date 30th December 2022 (Not yet recruiting). [NCT04611802].

VACCINE PLATFORM: Protein Subunit/ Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M.

BRIEF SUMMARY:

A Phase 3, Randomized, Observer-Blinded, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) With Matrix-M1™ Adjuvant in Adult Participants ≥ 18 Years.

2 ARMS (in up to 30,000 participants)

- *Experimental:* SARS-CoV-2 rS/Matrix-M1 Adjuvant (2 doses of 5 µg SARS-CoV-2 rS + 50 µg Matrix-M1 adjuvant (co-formulated), on Days 0 and 21).

- *Placebo Comparator:* Placebo (2 doses of Placebo (Saline) on Days 0 and 21).

OUTCOME MEASUREMENTS

Vaccine efficacy, immune response, and safety of a coronavirus disease 2019 (COVID-19) vaccine SARS-CoV-2 rS with Matrix-M1 adjuvant in adults 18 years and older in the United States and Mexico.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known. Phase 3 Recruiting

IV. VACCINE NAME: RECOMBINANT NOVEL CORONAVIRUS VACCINE (CHO CELLS)

MANUFACTURER: Anhui Zhifei Longcom Biologic Pharmacy Co., Ltd., CHINA

AVAILABILITY: Not available. Phase I study started on 22nd June 2020, primary completion date 22nd October 2020 and study completion date 20th September 2021. [NCT04445194]

VACCINE PLATFORM: Protein Subunit Adjuvanted recombinant protein (RBD-Dimer) expressed in CHO cells.

BRIEF SUMMARY:

A Multi-center, Double-blind, Randomized, Placebo Parallel Controlled, Safety and Tolerability Phase I Clinical Trial of Recombinant Novel Coronavirus Vaccine (CHO Cells) in Healthy People Between 18 and 59 Years of Age.

THREE TREATMENT GROUPS

- *Experimental:* 20 subjects, negative for SARS-COV-2 and fluorescent RT-PCR nucleic acids, administered low-dose vaccine by intramuscular injection.
- *Experimental:* 20 subjects negative for SARS-COV-2 and fluorescent RT-PCR nucleic acids, administered high-dose vaccine by intramuscular injection.

- *Placebo Comparator*: 10 subjects, negative for SARS-COV-2 and fluorescent RT-PCR nucleic acids, administered placebo by intramuscular injection.

The first stage randomized participants in the low-dose group (20 cases) and the placebo group (5 cases) evaluated for 7 days. After the 7-day safety data was evaluated and agreed by the DSMB, the second-stage study was conducted. Into the high-dose group (20 cases) and placebo group (5 cases) subjects; follow-up to 30 days, after the safety assessment by the investigator and consent,

then inoculate the second dose. Observation was performed for 1.0 hour after the second dose. The researchers conducted a safety evaluation and agreed to follow-up after discharge.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

V. VACCINE NAME: RECOMBINANT SARS-COV-2 VACCINE (CHO CELL)

Manufacturer: Anhui Zhifei Longcom Biopharmaceutical/Institute of Microbiology, Chinese Academy of Sciences

AVAILABILITY: Not available. [NCT04636333].

VACCINE PLATFORM: Protein Subunit/Adjuvant recombinant protein (RBD-Dimer) expressed in CHO cells.

BRIEF SUMMARY:

Phase I, randomized, placebo-controlled, double-blind study/Recruiting Safety and Immunogenicity of a Recombinant COVID-19 Vaccine (CHO Cell) in Healthy Population Aged 18 Years and Older.

Screening period is 1 week prior to randomization (Day -7 to Day -1), and each dose of either SARS-CoV-2 vaccine (CHO Cell) or placebo will be given intramuscularly on Day 0 and Day 14 for a two-dose regimen, or on Day 0, Day 14, and Day 28 for a three-dose regimen.

Subjects ≥18 years old and ≤ 59 years old will be enrolled in adult group, and healthy elderly population >59 years old will be enrolled in elderly group. After adult group completes the follow-up 7 days after first vaccination, elderly group will be recruited. After randomization, each participant would be followed up for approximately 13 months.

TWELVE TREATMENT GROUPS

- *Experimental:* Middle-dose vaccine (18-59 years) & Two dose regimen. Two doses of middle-dose experimental vaccine at the schedule of day 0, 14. *Intervention:* Biological: Two doses of middle-dose recombinant SARS-CoV-2 vaccine (CHO Cell) at the schedule of day 0, 14.
- *Experimental:* Middle-dose vaccine (18-59 years) & Three dose regimen. Three doses of middle-dose experimental vaccine at the schedule of day 0, 14 28.

Intervention: Biological: Three doses of middle-dose recombinant SARS-CoV-2 vaccine (CHO Cell) at the schedule of day 0, 14, 28.

- *Experimental:* High-dose vaccine (18-59 years) & Two dose regimen. Two doses of high-dose experimental vaccine at the schedule of day 0, 14. *Intervention:* Biological: Two doses of high-dose recombinant SARS-CoV-2 vaccine (CHO Cell) at the schedule of day 0, 14.
- *Experimental:* High-dose vaccine (18-59 years) & Three dose regimen. Two doses of High-dose vaccine at the schedule of day 0, 14, 28. *Intervention:* Biological: Three doses of high-dose recombinant SARS-CoV-2 vaccine (CHO Cell) at the schedule of day 0, 14, 28.
- *Experimental:* Middle-dose vaccine (> 59 years) & Three dose regimen. Three doses of middle-dose experimental vaccine at the schedule of day 0, 14, 28. *Intervention:* Biological: Three doses of middle-dose recombinant SARS-CoV-2 vaccine (CHO Cell) at the schedule of day 0, 14, 28.
- *Experimental:* High-dose vaccine (> 59 years) & Three dose regimen. Three doses of high-dose experimental vaccine at the schedule of day 0, 14, 28. *Intervention:* Biological: Three doses of high-dose recombinant SARS-CoV-2 vaccine (CHO Cell) at the schedule of day 0, 14, 28.
- *Placebo Comparator:* Middle-dose placebo (18-59 years) & Two dose regimen. Two doses of middle-dose placebo at the schedule of day 0, 14. *Intervention:* Biological: Two doses of placebo at the schedule of day 0, 14 #middle-dose group#
- *Placebo Comparator:* Middle-dose placebo (18-59 years) & Three dose regimen. Three doses of middle-dose placebo at the schedule of day 0, 14, 28. *Intervention*: Biological: Three doses of placebo at the schedule of day 0, 14, 28 #middle-dose group#
- *Placebo Comparator:* High-dose placebo (18-59 years) & Two dose regimen. Two doses of high-dose placebo at the schedule of day 0, 14. *Intervention:* Biological: Two doses of placebo at the schedule of day 0, 14 #High-dose group#
- *Placebo Comparator*: High-dose placebo (18-59 years) & Three dose regimen. Three doses of high-dose placebo at the schedule of day 0, 14, 28. *Intervention:* Biological: Three doses of placebo at the schedule of day 0, 14, 28 #High-dose group#
- *Placebo Comparator:* Middle-dose placebo (> 59 years) & Three dose regimen. Three doses of high-dose placebo at the schedule of day 0, 14, 28. *Intervention:* Biological: Three doses of placebo at the schedule of day 0, 14, 28 #middle-dose group#
- *Placebo Comparator*: High-dose placebo (> 59 years) & Three dose regimen. Three doses of high-dose placebo at the schedule of day 0, 14, 28. *Intervention:*

Biological: Three doses of placebo at the schedule of day 0, 14, 28 #High-dose group#

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known. Phase 3 Recruiting

VI. VACCINE NAME: RECOMBINANT NEW CORONAVIRUS VACCINE (CHO CELLS)

MANUFACTURER: Anhui Zhifei Longcom Biopharmaceutical/Institute of Microbiology, Chinese Academy of Sciences

AVAILABILITY: Not available. Phase 1 started on August 19, 2020; proposed completion date, December 31, 2021. [NCT04550351].

VACCINE PLATFORM: Protein Subunit/Adjuvant recombinant protein (RBD-Dimer) expressed in CHO cells

BRIEF SUMMARY:

A Randomized, Double-blind, Placebo-controlled Phase I Clinical Trial to Evaluate the Safety and Tolerability of Recombinant New Coronavirus **Vaccines** (CHO Cells) in Healthy People Aged 60 Years and Above.

THREE TREATMENT GROUPS

- Experimental: 20 subjects, negative for SARS-COV-2 and fluorescent RT-PCR nucleic acids, to be given low dose vaccine by intramuscular injection.
- Experimental: 20 subjects, negative for SARS-COV-2 and fluorescent RT-PCR nucleic acids, to be given high-dose vaccine by intramuscular injection.
- Placebo Comparator: 10 subjects, negative for SARS-COV-2 and fluorescent RT-PCR nucleic acids, to be given placebo by intramuscular injection.

OUTCOME MEASUREMENTS

To evaluate the safety and tolerability of low and high doses of recombinant new coronavirus vaccine (CHO cells) in healthy people aged 60 years and above.

Secondary outcome: to initially explore the immunogenicity and durability of different doses of recombinant new coronavirus vaccine (CHO cells).

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known. Phase 3 Recruiting

VII. VACCINE NAME: RECOMBINANT NEW CORONAVIRUS VACCINE (CHO CELL)

MANUFACTURER: Anhui Zhifei Longcom Biologic Pharmacy Co., Ltd./Phase 2

AVAILABILITY: Not available**.** Phase I trial started 12th July 2020, proposed completion date 15th December 2021. [NCT04466085].

VACCINE PLATFORM: Protein Subunit/ Adjuvant recombinant protein (RBD-Dimer) expressed in CHO cells

BRIEF SUMMARY:

A Randomized, Blinded, Placebo-controlled Trial to Evaluate the Immunogenicity and Safety of a Recombinant New Coronavirus Vaccine (CHO Cell) With Different Doses and Different Immunization Procedures in Healthy People Aged 18 to 59 Years.

SIX TREATMENT GROUPS

- *Experimental:* 150 subjects given 2 doses of low-dose vaccine *im* at 0 and 1 months.
- *Experimental:* 150 subjects given 2 doses of high-dose vaccine *im* on 0 and 1 months.
- *Placebo Comparator:* 150 subjects given 2 doses of placebo *im* on 0 and 1 months.
- *Experimental:* 150 subjects given 3 doses of low-dose vaccine *im* on 0, 1, and 2 months.
- *Experimental:* 150 subjects given 3 doses of high-dose vaccine *im* on 0, 1, and 2 months.
- *Placebo Comparator:* 150 subjects given 3 doses of placebo *im* at 0, 1, and 2 months.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known. Phase 3 Recruiting

VIII. VACCINE NAME: CHO CELL

MANUFACTURER: Anhui Zhifei Longcom Biologic Pharmacy Co., Ltd./Phase 3

AVAILABILITY: Not available. Phase 3 trial started 22nd November 2020: proposed completion date 31st December 2021. [ChiCTR2000040153].

VACCINE PLATFORM: Protein Subunit/ Adjuvanted recombinant protein (RBD-Dimer) expressed in CHO cells

BRIEF SUMMARY:

A randomized, double-blind, placebo-controlled phase III clinical trial of the effectiveness and safety of inoculation of recombinant new coronavirus vaccine (CHO cells) in the prevention of COVID-19 in people 18 years and older.

TWO TREATMENT GROUPS

- Intervention: test vaccine and placebo control

OUTCOME MEASUREMENTS

To evaluate the protective efficacy and safety of recombinant new coronavirus vaccine (CHO cells) in preventing any severity of COVID-19 in people 18 years of age and above.

Secondary purpose: Evaluate the protective efficacy of recombinant new coronavirus vaccine (CHO cell) in preventing severe COVID-19 and above in people aged 18 years and above.

To evaluate the immunogenicity and immune durability of the recombinant new coronavirus vaccine (CHO cells) in people 18 years of age and older.

To evaluate the protective efficacy of the recombinant new coronavirus vaccine (CHO cell) in the emergency vaccination of people aged 18 years and above to prevent COVID-19 of any severity.

To evaluate the protective efficacy of the recombinant new coronavirus vaccine (CHO cells) in preventing any severity of COVID-19 in people of different age groups (18-59 years old, 60 years old and above).

Exploratory purpose: Explore the immunological alternative indicators of recombinant new coronavirus vaccine (CHO cells) to prevent COVID-19 in people aged 18 and above.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known. Phase 3 Recruiting

IX. VACCINE NAME: KBP-201 COVID-19

MANUFACTURER: Kentucky BioProcessing, Inc.

AVAILABILITY: Not available. Phase 1/2 proposed start date 28th December 2020; proposed completion date, 6th May 2021. [NCT04473690].

VACCINE PLATFORM: Protein Subunit/RBD-based.

BRIEF SUMMARY:

A First-in-human, Observer-blinded, Randomized, Placebo-controlled, Parallel Group Study to Evaluate the Safety and Immunogenicity of KBP-COVID-19 SARS-CoV-2 Vaccine with Adjuvant in Healthy Seronegative Adults Aged 18-49 and 50-70.

OUTCOME MEASUREMENTS

To evaluate the safety and immunogenicity of KBP-COVID-19 vaccine in healthy CoV-2seronegative adult subjects in 2 age groups, Part A (18-49 years) and Part B (50-70 years).

THREE TREATMENT GROUPS

- *Experimental:* Low-dose KBP-COVID-19. Two age groups. Part A (18-49 years). Part B (50-70 years).
- *Experimental:* High Dose KBP-COVID-19. Two age groups. Part A (18-49 years). Part B (50-70 years).
- *Placebo Comparator:* Placebo. Two age groups. Part A (18-49 years). Part B (50-70 years).

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known. Phase 3 Recruiting

X. VACCINE NAME: SARS-COV-2 RECOMBINANT PROTEIN

MANUFACTURER: Sanofi Pasteur/GSK

AVAILABILITY: Not available. Phase 1/2 trials started 3rd September 2020, proposed completion date, October 2021. [NCT04537208]

VACCINE PLATFORM: Protein Subunit/ S protein (baculovirus production)

BRIEF SUMMARY

Randomized, quadruple-blind, controlled trial to evaluate immunogenicity and Safety of SARS-CoV-2 Recombinant Protein Vaccine Formulations (With or Without Adjuvant) in Healthy Adults 18 Years of Age and Older.

OUTCOME MEASUREMENTS

- Describe neutralizing antibody profile at Day 1, Day 22, and Day 36 for each arm.
- Safety profile in each age group and each arm up to 12 months post-injection.

  Secondary outcomes:
- Describe binding antibody profile at Day 1, Day 22, Day 36, Day 181 (Cohort 1) or Day 202 (Cohort 2), and Day 366 (Cohort 1) or Day 387 (Cohort 2) of each arm.
- Describe neutralizing antibody profile at Day 181 (Cohort 1) or Day 202 (Cohort 2) and at Day 366 (Cohort 1) and Day 387 (Cohort 2) of each arm.
- Describe occurrence of virologically confirmed COVID-19-like illness and serologically confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.
- Evaluate the correlation / association between antibody responses to SARS-CoV-2 Recombinant Protein and the risk of COVID-19-like illness and/or serologically confirmed SARS-CoV-2 infection.

TWENTY-ONE TREATMENT GROUPS

- *Experimental:* Group 1 (18 - 49 years of age). 1 injection of SARS-CoV-2 vaccine formulation 1 with adjuvant 1 at Day 1.
- *Experimental:* Group 2 (18 - 49 years of age). 1 injection of SARS-CoV-2 vaccine formulation 1 with adjuvant 2 at Day 1.
- *Experimental:* Group 3 (18 - 49 years of age). 1 injection of SARS-CoV-2 vaccine formulation 2 with adjuvant 1 at Day 1.

- *Experimental:* Group 4 (18 - 49 years of age). 1 injection of SARS-CoV-2 vaccine formulation 2 with adjuvant 2 at Day 1.
- *Placebo:* Group 5 (18 - 49 years of age). 1 injection of placebo (0.9% normal saline) at Day 1.
- *Experimental:* Group 6 (18 - 49 years of age). 2 injections of SARS-CoV-2 vaccine formulation 1 with adjuvant 1 at Day 1 and Day 22.
- *Experimental:* Group 7 (18 - 49 years of age). 2 injection of SARS-CoV-2 vaccine formulation 1 with adjuvant 2 at Day 1 and Day 22.
- *Experimental:* Group 8 (18 - 49 years of age). 2 injections of SARS-CoV-2 vaccine formulation 2 with adjuvant 1 at Day 1 and Day 22.
- *Experimental:* Group 9 (18 - 49 years of age). 2 injections of SARS-CoV-2 vaccine formulation 2 with adjuvant 2 at Day 1 and Day 22.
- *Experimental:* Group 10 (18 - 49 years of age). 2 injections of SARS-CoV-2 vaccine formulation 2 without adjuvant at Day 1 and Day 22.
- *Placebo Comparator:* Group 11 (18 - 49 years of age). 2 injections of placebo at Day 1 and Day 22
- *Experimental:* Group 12 (50 years of age and older). 1 injection of SARS-CoV-2 vaccine formulation 1 with adjuvant 1 at Day 1.
- *Experimental:* Group 13 (50 years of age and older). 1 injection of SARS-CoV-2 vaccine formulation 1 with adjuvant 2 at Day 1
- *Experimental:* Group 14 (50 years of age and older). 1 injection of SARS-CoV-2 vaccine formulation 2 with adjuvant 1 at Day 1
- *Experimental:* Group 15 (50 years of age and older). 1 injection of SARS-CoV-2 vaccine formulation 2 with adjuvant 2 at Day 1.
- *Placebo Comparator:* Group 165 (50 years of age and older). 1 injection of placebo at Day 1.
- *Experimental:* Group 17 (50 years of age and older). 2 injections of SARS-CoV-2 vaccine formulation 1 with adjuvant 1 at Day 1 and Day 22.
- *Experimental:* Group 18 (50 years of age and older). 2 injections of SARS-CoV-2 vaccine formulation 1 with adjuvant 2 at Day 1 and Day 22.
- *Experimental:* Group 19 (50 years of age and older). 2 injections of SARS-CoV-2 vaccine formulation 2 with adjuvant 1 at Day 1 and Day 22.
- *Experimental:* Group 20 (50 years of age and older). 2 injections of SARS-CoV-2 vaccine formulation 2 with adjuvant 2 at Day 1 and Day 22.

- *Placebo Comparator:* Group 21 (50 years of age and older). 2 injections of placebo (0.9% normal saline) at Day 1 and Day 22.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

XI. VACCINE NAME: BECT062/COVID-19

MANUFACTURER: Biological E Ltd / India/ Phase 1/2

AVAILABILITY: Not available. Start date 16th November 2020, no declared completion date. [CTRI/2020/11/029032]

VACCINE PLATFORM: Protein Subunit/Adjuvanted protein subunit (RBD)

BRIEF SUMMARY:

A prospective, open-label, randomiszd phase-I seamlessly followed by phase-II study to assess the safety, reactogenicity and immunogenicity of Biological E's novel Covid-19 vaccine containing Receptor Binding Domain of SARS-CoV-2 for protection against Covid-19 disease when administered intramuscularly in a two-dose schedule (0, 28D) to healthy volunteers.

ONE TREATMENT GROUP

Intervention: Biological E's novel Covid-19 vaccine containing Receptor Binding Domain of SARS-CoV-2. Four formulations, BECOV2D, BECOV2C, BECOV2B and BECOV2A. Dose: 0.5ml, by intramuscular injection, Frequency: Two doses at Day 0 and Day 28.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

XII. VACCINE NAME: SCB-2019

MANUFACTURER: Clover Biopharmaceuticals Inc.,Australia/GSK/Dynavax /Phase 1/Recruiting

AVAILABILITY: Not available. Phase 1 started 19th June 2020, proposed completion date 20th October 2020. [NCT04405908].

VACCINE PLATFORM: Protein Subunit/Native like Trimeric subunit Spike Protein vaccine

BRIEF SUMMARY:

A Phase 1, Randomized, Double-blind, Placebo-controlled, First-in-human Study to Evaluate the Safety and Immunogenicity of SCB 2019, a Recombinant SARS-CoV-2 Trimeric S Protein Subunit Vaccine for COVID-19 in Healthy Volunteers.

OUTCOME MEASUREMENTS

- To assess safety, reactogenicity and immunogenicity of SCB-2019 at multiple dose levels, administered as 2 injections IM in healthy subjects.

- Each study vaccine dose level will be evaluated with and without adjuvant.

FIFTEEN TREATMENT GROUPS

- *Active Comparator:* Adult Group 1. Adult healthy subjects (18 to 54 years of age, inclusive) receive SCB-2019 3 µg.
- *Active Comparator*: Adult Group 2. Adult healthy subjects (18 to 54 years of age, inclusive) receive SCB-2019 3 µg with AS03 adjuvant.
- *Active Comparator:* Adult Group 3. Adult healthy subjects (18 to 54 years of age, inclusive) receive SCB-2019 3 µg with CpG 1018 plus Alum adjuvant.
- *Active Comparator:* Adult Group 4. Adult healthy subjects (18 to 54 years of age, inclusive) receive SCB-2019 9 µg.
- *Active Comparator:* Adult Group 5. Adult healthy subjects (18 to 54 years of age, inclusive) receive SCB-2019 9 µg with AS03 adjuvant.
- *Active Comparator:* Adult Group 6. Adult healthy subjects (18 to 54 years of age, inclusive) receive SCB-2019 9 µg with CpG 1018 plus Alum adjuvant.
- *Active Comparator:* Adult Group 7. Adult healthy subjects (18 to 54 years of age, inclusive) receive SCB-2019 30 µg.
- *Active Comparator:* Adult Group 8. Adult healthy subjects (18 to 54 years of age, inclusive) receive SCB-2019 30 µg with AS03 adjuvant.
- *Active Comparator:* Adult Group 9. Adult healthy subjects (18 to 54 years of age, inclusive) receive SCB-2019 30 µg with CpG 1018 plus Alum adjuvant.
- *Active Comparator:* Elderly Group 10. Elderly healthy subjects (55 to 75 years of age, inclusive) receive SCB-2019 3 µg with AS03 adjuvant.
- *Active Comparator:* Elderly Group 11. Elderly healthy subjects (55 to 75 years of age, inclusive) receive SCB-2019 3 µg with CpG 1018 plus Alum adjuvant.

- *Active Comparator:* Elderly Group 12. Elderly healthy subjects (55 to 75 years of age, inclusive) receive SCB-2019 9 µg with AS03 adjuvant.
- *Active Comparator:* Elderly Group 13. Elderly healthy subjects (55 to 75 years of age, inclusive) receive SCB-2019 9 µg with CpG 1018 plus Alum adjuvant.
- *Active Comparator*: Elderly Group 14. Elderly healthy subjects (55 to 75 years of age, inclusive) receive SCB-2019 30 µg with AS03 adjuvant.
- *Active Comparator:* Elderly Group 15. Elderly healthy subjects (55 to 75 years of age, inclusive) receive SCB-2019 30 µg with CpG 1018 plus Alum adjuvant.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

XIII. VACCINE NAME: MONOVALENT RECOMBINANT COVID19 VACCINE (COVAX19)

MANUFACTURER: Vaxine Pty Ltd / Phase 1/Recruiting

AVAILABILITY: Not available. Phase I trial started on 30th June 2020, proposed completion date 1st July 2021. [NCT04453852].

VACCINE PLATFORM: Protein Subunit. Recombinant spike protein with Advax™ adjuvant

BRIEF SUMMARY:

A Randomised, Controlled, Phase 1 Study to Evaluate the Safety and Immunogenicity of a Candidate Adjuvanted Recombinant Protein SARS-COV-2 Vaccine in Healthy Adult Subjects

TWO TREATMENT GROUPS

- *Experimental:* Group A. Spike antigen (25ug) + 15 mg Advax-2 adjuvant
- *Placebo Comparator:* Group B. Saline

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

XIV. VACCINE NAME: MVC-COV1901

MANUFACTURER: Medigen Vaccine Biologics Corporation/NIAID/Dynavax

AVAILABILITY: Not available. Started on 07 October 2020, proposed completion 30th January 2021, estimated study completion date, 30th June 2021. Phase 2 studies to start early 2021 with about 3,000 healthy volunteers in Taiwan and Vietnam. [NCT04487210]

VACCINE PLATFORM: Protein subunit.

BRIEF OVERVIEW

A phase I prospective, open-labeled, single-center study to evaluate the safety and immunogenicity of MVC-COV1901 in 45 healthy male and female Taiwanese volunteers. This study is a dose escalation study with three separate arms for subjects at the age of ≥20 and <50 years. The vaccination schedule consists of two doses of MVC-COV1901 for each study subject, administered by intramuscular (IM) injection 0.5mL in the deltoid region of non-dominant arm preferably 28 days apart, on Day 1 and Day 29.

OUTCOME MEASUREMENTS

- Safety of MVC-COV1901 [Time Frame: Day 1 to 28 days after second vaccination]
- Incidence of solicited adverse events (AEs) after vaccination, Incidence of unsolicited AEs and other AEs after vaccination, Incidence of laboratory abnormality after vaccination, Incidence of adverse event of special interest (AESI) and serious adverse events (SAEs) after vaccination

SECONDARY MEASURES

- Immunogenicity (neutralizing antibody titers and antigen specific binding antibody titers) [Time Frame:14 days, 28 days after each vaccination, and 180 days after 2nd vaccination]
- Geometric mean titer (GMT), Seroconversion rate (SCR), and GMT ratio.
- Immunogenicity (antigen specific cellular immune responses) [Time Frame: 28 days and 180 days after 2nd vaccination].
- The positive rate of cellular mediated immune response.
- Safety of MVC-COV1901 [Time Frame: Day1 to Day 209].
- Incidence of other adverse events, Incidence of adverse event of special interest (AESI) and serious adverse events (SAEs) within the study period.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

XV. VACCINE NAME: FINLAY- FR-2 ANTI SARS-COV-2

MANUFACTURER: Finlay Institute of Vaccines (IFV), Cuba

AVAILABILITY: Not available. Phase I trial started 29th October 2020 in Cuba, proposed completion January 2021.

VACCINE PLATFORM: Protein subunit. rRBD produced in CHO-cell chemically conjugate to tetanus toxoid.

BRIEF SUMMARY:

Phase 1, open, uncontrolled, sequential and adaptive study in Cuba. In 40 healthy male and female volunteers aged 19 to 59.

OUTCOME MEASUREMENTS

- Evaluate the safety profile of two formulations of different strengths of the vaccine candidate in a two-dose scheme (0-28).
- Evaluate the reactogenicity of two formulations of different strengths of the vaccine candidate in a two-dose scheme (0-28).
- Explore the immunogenicity of two formulations of different strengths of the vaccine candidate in two-dose scheme (0-28).

Two treatment groups

- *Group 1*- FINLAY-FR-2 low-dose of RBD conjugated + adjuvant; 0.5 mL, intramuscularly (IM). Treatment scheme: 0-28 days.
- *Group 2*- FINLAY-FR-2 high-dose of RBD conjugated + adjuvant; 0.5 mL; Treatment scheme: 0-28 days.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

XVI. VACCINE NAME: FINLAY- FR-1 ANTI SARS-COV-2

MANUFACTURER: Finlay Institute of Vaccines (IFV), Cuba

AVAILABILITY: Not available. Phase I/II multi-center trial started 24th August 2020, proposed completion date January 2021.

VACCINE PLATFORM: Protein subunit. RBD + Adjuvant.

BRIEF SUMMARY:

Phase I/II study, randomized, controlled, adaptive, double-blind and multicenter trial in healthy adults in two age groups: each arm will form two age groups, 19-59 years old, 60-80 years old.

OUTCOME MEASUREMENTS

- Evaluate the safety profile of the vaccine candidate applied in two-dose 2 schemes.
- Evaluate the reactogenicity of the vaccine candidate applied in two-dose 3 schemes.
- Evaluate the immunogenicity of the vaccine candidate applied in two-dose 4 schemes.
- Compare the immune response of formulations with different dosage levels.

THREE TREATMENT GROUPS

- FINLAY-FR-1 (Experimental): 10 g dose of RBD+adjuvant; 0.5 mL, intramuscularly. Treatment scheme: 0-28 days.
- FinLAY-FR-1 (Experimental): 20g dose of RBD + adjuvant; 0.5 mL; intramuscularly. Treatment scheme: 0-28 days.
- VA-MENGOC-BC® (Control): Dose of 0.5 mL of the product intramuscularly. Treatment scheme: 0-28 days.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

XVII. VACCINE NAME: IMP COVAC-1 (SARS-COV-2 HLA-DR PEPTIDES, XS15 EMULSIFIED IN MONTANIDE ISA 51 VG)

MANUFACTURER: University Hospital Tuebingen, Germany

AVAILABILITY: Not available. Phase I trial started on 27th November 2020, estimated completion date 20th December 2021. [NCT04546841]

VACCINE PLATFORM: Single dose, SARS-CoV-2 HLA-DR multipeptide cocktail in adjuvant (TLR1/2 ligand XS15).

BRIEF SUMMARY:

Phase I, open-label, single-center study. In 36 healthy adults over 18 years old. Part I: 18-55 years (n=12); Part II: 56-74 (n=12); Part III: ≥ 75 (n=12). A single vaccination administered subcutaneously (*sc*) to the abdominal skin.

THREE TREATMENT GROUPS

- *Part I:* Age 18-55 at the time of screening, n=12
- *Part II:* Age 56-74 years at the time of screening, n=12
- *Part III:* Age ≥ 75 years at the time of screening, n=12

OUTCOME MEASUREMENTS

- Safety (at Day 28)
- CoVac-1 specific T-cell response (at Day 28)

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

XVIII. VACCINE NAME: UB-612 - MULTITOPE PEPTIDE-BASED S1-RBDPROTEIN VACCINE

MANUFACTURER: COVAXX /United Biomedical Inc. Asia

AVAILABILITY: Not available. Phase 3 trial started on 25th September 2020, estimated completion 31st August 2021.

VACCINE PLATFORM: Subunit expressed in CHO cells (Chinese Academy of Military Sciences)

BRIEF SUMMARY:

Phase I, open-label, non-randomized, dose-escalation study in Taiwan. In 60 healthy adults aged 20 to 55 years to evaluate the safety, tolerability and immunogenicity of 3 ascending doses of UB-612 COVID-19 vaccine in healthy adults. Up to 60 subjects (20 subjects per group) will be enrolled into this study. Subjects in each group will be enrolled to receive two doses of UB-612 vaccine at 28-day interval (Day 0 and Day 28).

THREE TREATMENT GROUPS

- Group A (Low dose): 20 subjects to receive low dose of UB-612 vaccine.
- Group B (Medium dose): 20 subjects to receive medium dose of UB-612 vaccine.
- Group C (High dose): 20 subjects to receive high dose of UB-612 vaccine.

Outcome MEASUREMENTS

Safety [Time Frame: within 7 days post vaccination]

- Occurrence of adverse reactions
- Percentage of subjects with ≥ Grade 3 adverse events

Immunogenicity [Time Frame: Day 14, 28, 42, 56, 112, and 196]

- Geometric mean titer (GMT) of antigen-specific antibody (Anti-S1-RBD)
- Seroconversion rate (SCR) of antigen-specific antibody (Anti-S1-RBD)
- Geometric mean fold increase of antigen-specific antibody (Anti-S1-RBD)

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

XIX. VACCINE NAME: SUBUNIT EXPRESSED IN CHO CELLS

AVAILABILITY: Not available. Phase 3 trial started on 22nd November 2020, estimated completion 31st December 2021. [ChiCTR2000040153]

VACCINE PLATFORM: Protein Subunit expressed in CHO cells.

BRIEF SUMMARY:

Phase 3, randomized, double-blind, placebo-controlled trial. Recombinant new coronavirus vaccine (CHO cells). In adults stratified by age between over 18 – 59 years, and 60 years old.

OUTCOME MEASUREMENTS

To evaluate the protective efficacy and safety of recombinant new coronavirus vaccine (CHO cells) in preventing any severity of COVID-19 in people 18 years of age and above.

To evaluate SARS-CoV-2 neutralizing antibody and RBD protein binding antibody (IgG).

SECONDARY*:*

- Evaluate protective efficacy of recombinant new coronavirus vaccine (CHO cell) in preventing severe COVID-19 in people aged 18 years and older.
- Evaluate immunogenicity and immune durability of recombinant new coronavirus vaccine (CHO cells) in people 18 years of age and older.
- Evaluate protective efficacy of recombinant new coronavirus vaccine (CHO cell) in the emergency vaccination of people aged 18 years and older to prevent COVID-19 of any severity.
- Evaluate protective efficacy of recombinant new coronavirus vaccine (CHO cells) in preventing any severity of COVID-19 in people of different age groups (18-59 years old, 60 years old and older).
- Explore the immunological alternative indicators of recombinant new coronavirus vaccine (CHO cells) to prevent COVID-19 in people aged 18 and above.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

XX. VACCINE NAME: UQ-1-SARS-COV2-SCLAMP

MANUFACTURER: University of Queensland/CSL/Seqirus)

AVAILABILITY: Not available. Started 13th July 2020, **trial terminated**. [ACTRN12620000674932]

VACCINE PLATFORM: Protein subunit. Vaccine uses two fragments of a protein known as glycoprotein 41 (gp41), which is found in the human immunodeficiency virus (HIV) but is not able to infect people or replicate. On its own, the SARS-CoV-2 spike protein is unstable and is 'locked' into shape by the HIV glycoprotein.

BRIEF SUMMARY:

Phase 1, randomized, double-blinded, placebo-controlled, dose-escalation single center study in Australia. In 120 healthy male and female volunteers aged 18 to 55. Two doses, 28 days apart.

OUTCOME MEASUREMENTS

To assess the safety and tolerability of SARS-CoV-2 Sclamp vaccine compared to placebo by evaluating:

- frequency, duration and intensity of solicited local adverse events (AEs), including pain, redness, induration.
- frequency, duration and intensity of solicited systemic AEs, including fever, nausea, chills, diarrhoea, headache, fatigue, myalgia.
- frequency, duration, intensity, and relatedness of unsolicited AEs through to Day 57.

Solicited AEs will be assessed by severity score, frequency, duration and intensity by FDA toxicity scoring.

FOUR TREATMENT GROUPS

- *Treatment A* (Cohorts 1 & 4): SARS-CoV-2 Sclamp vaccine 1 x 5 µg in 0.5 ml suspension, administered as two separate doses at least 28 days apart.
- *Treatment B* (Cohorts 2 & 5): SARS-CoV-2 Sclamp vaccine 1 x 15 µg in 0.5 ml suspension, administered as two separate doses, at least 28 days apart.
- *Treatment C* (Cohorts 3 & 6): SARS-CoV-2 Sclamp vaccine 1 x 45 µg in 0.5 ml suspension, administered as two separate doses at least 28 days apart.
- *Treatment D* (Cohort 3): SARS-CoV-2 Sclamp vaccine 1 x 45 µg in 0.5 ml suspension, followed by placebo administered as the second dose at least 28 days apart.

SAFETY: NOT KNOWN.

OVERALL QUALITY OF EVIDENCE: Not known.

STATUS: TERMINATED – Robust immune response and strong safety profile, BUT false-positive HIV tests.

6.1.6 Virus-Like Peptide Vaccine

These vaccines are multimeric structures assembled from viral structural proteins that can directly stimulate immune cells by mimicking the three-dimensional conformation of native virus.

I. VACCINE NAME: VLP

MANUFACTURER: Medicago Inc.

AVAILABILITY: Not available. Trial started July 2020.

VACCINE PLATFORM: Plant-derived VLP adjuvanted with AS03.

BRIEF SUMMARY:

A Phase 1, randomized, partially blinded, dose-escalating study to Assess the Safety, Tolerability, and Immunogenicity of a Recombinant Coronavirus-Like Particle COVID-19 Vaccine in Adults 18-55 Years of Age. Phase I randomized, partially blinded, prime-boost, staggered dose-escalation study. The vaccine was administered at 3 dose levels adjuvanted or unadjuvanted. [NCT04450004]

A Phase 2/3 Randomized, Observer-Blind, Placebo-Controlled, Phase 2/3 Study to Assess the Safety, Efficacy, and Immunogenicity of a Recombinant Coronavirus-Like Particle COVID-19 Vaccine in Adults 18 Years of Age or Older. [NCT04636697]. Subjects will receive 2 doses of vaccine adjuvanted 21 days apart compared with placebo.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

II. VACCINE NAME: (RBD) SARS-COV-2 (COVID-19) HEPATITIS B SURFACE ANTIGEN (HBSAG) VIRUS LIKE PARTICLE (VLP)

MANUFACTURER: SpyBiotech/Serum Institute of India

AVAILABILITY: Not available. Started August 2020. [ACTRN12620000817943]

VACCINE PLATFORM: RBD-HBsAg VLPs

BRIEF SUMMARY:

A randomized, observer-blind, placebo-controlled, Phase I/II study to evaluate the safety, reactoger and immunogenicity of Receptor Binding Domain (RBD) SARS-CoV-2 (COVID-19) Hepatitis B surface antigen (HBsAg) virus like particle (VLP) Vaccine in Healthy Adults

Phase I – 2 doses of vaccine given 28 days apart compared with placebo.

Phase II – single dose of vaccine with placebo 28 days apart, 2 doses of vaccine 28 days apart compared with placebo.

6.1.7 Live-Attenuated Vaccine

These vaccines are a weakened form of the live virus but does not cause infection. They induce the same response as natural infection, thus triggering an immune response.

I. VACCINE NAME: COVI-VAC

MANUFACTURER: Codagenix/Serum Institute of India

AVAILABILITY: Not available. Phase I trial started in December 2020. [NCT04619628]

VACCINE PLATFORM: Codon deoptimized live attenuated vaccines.

BRIEF SUMMARY:

First-in-human, Randomised, Double-blind, Placebo-controlled, Dose-escalation Study in Healthy Young Adults Evaluating the Safety and Immunogenicity of COVI-VAC, a Live Attenuated Vaccine Candidate for Prevention of COVID-19.

Phase 1 clinical trial – randomized, double-blind, placebo-controlled, dose escalation study. Approximately 48 participants will be enrolled into 1 of 3 groups. Each group will receive 2 doses of COVI-VAC 28 days apart, 2 doses of placebo 28 days apart or 1 dose of COVI-VAC and 1 dose of placebo 28 days apart.

SAFETY: Not known.

OVERALL QUALITY OF EVIDENCE: Not known.

6.2 Appendix 2 :Planning Models

- WHO. Guide to Tailoring Immunization Programs (TIP) for infant and child vaccination [1]. The TIP principles apply to communicable, non-communicable, and emergency planning where behavioural decisions influence outcomes [8] https://www.who.int/immunization/programmes_systems/Global_TIP_overview_July2018.pdf?ua=1
- European Centre for Disease Control (ECDC). Technical Guide to Social Marketing https://www.ecdc.europa.eu/en/publications-data/social-marketing-guide-public-healthprogramme-managers-and-practitioners
- WHO. Improving vaccination demand and addressing hesitancy. https://www.who.int/immunization/programmes_systems/vaccine_hesitancy/en/
- ECOM: Effective Communication in Outbreak Management (ECOM) [9]. The E.U. funded ECOM project brings together multiple disciplines to develop an evidence-based behavioural and communication package for health professionals and agencies throughout Europe in case of significant outbreaks of infectious diseases. http://ecomeu.info/
- Tell Me. Review of population behaviour and communication during pandemics: https://www.tellmeproject.eu/
- Human Center Design for Health. A comprehensive set of tools developed by UNICEF to apply the human-centered design approach to challenges facing health services, with a particular emphasis on demand for immunization and health services. https://www.hcd4health.org/resources
- Social Science Research for Vaccine Deployment in Epidemic Outbreaks. A practical guide to using social science research and insights to better understand social, behavioural, cultural, community and political dynamics as part of efforts to introduce vaccines in epidemic outbreak settings. https://opendocs.ids.ac.uk/opendocs/bitstream/handle/20.500.12413/15431/PracApproach%206.pdf?sequence=2&isAllowed=y

Further generic planning guidance can be found at:

- Building Better Health: A Handbook for Behavioural Change. “The Handbook blends proven disease prevention practices and behavioural science principles into a one-of-a-kind, hands-on manual.” [10] (p. xiii).

- CDCYNERGY Planning Tool for Social Marketing. Centers for Disease Control and Prevention planning tool for social marketing, Atlanta, GA. Also available is CDCynergy “Lite”, intended for those who have previous social marketing experience and those who are familiar with the full CDCYNERGY edition. https://www.thecommunityguide.org/resources/cdcynergy
- Applying Behavioural Insights—Simple Ways to Improve Health Outcomes. A tool for the application of behavioural insights to improving health outcomes from the World Innovation Summit for Health. https://www.imperial.ac.uk/media/imperial-college/institute-of-global-health-innovation/ Behavioral_Insights_Report-(1).pdf