CT Application(s) Summary Report

- **Protocol title:** Phase 1 Clinical Trial to Evaluate the Safety, Tolerability, and Immunogenicity of Inactivated SARS-CoV-2 Vaccine Against COVID-19 in Healthy Adults.
- **Protocol code number:** COVID_VACC_1
- ***Public Registry Number:*** NCT04830800
- **Version:** 4.1
- **Date:** 31/10/2021

- **Investigational Medicinal Product being tested:**

Biological ■ **Pharmaceutical** ☐ **Innovative** ☐

Herbal medicine ☐ **Medical device** ☐

- **Sponsor:** National Research Centre (NRC)
- **Indication:** Protection against COVID-19, An acute respiratory disease, caused by a novel Coronavirus (SARS-CoV-2).
- **Investigator's brochure (IB)**

Version: 5.0
Date: 12/10/2021

- **Name of all Sites:** Medical Research Centre of Excellence, National Research Centre
- **Name of PI(s):** Dr Osama Azmy

- **EDA approval date:** 09/11/2021

- **Summary of pre-clinical studies:**

A. Nonclinical Pharmacology

The results of pre-clinical studies conducted in China on inactivated virus vaccines have demonstrated a good safety profile and effective protection against COVID-19 infection in tested animals.

➢ **Primary Pharmacodynamics:**

1- **CoronaVac (formerly PiCoVacc Vaccine):**

This study was conducted to evaluate the immunogenicity and protective efficacy of the inactivated SARS-CoV-2 vaccine candidate (PiCoVacc, CoronaVac) in relevant animal models: **BALB/c mice**, **Rats**, and **Rhesus macaques**", using Intramuscular (IM) according to the following dosing schedule (Mice: Days 0 and 7, and Macaques: Days 0, 7, and 14. The inactivated SARS-CoV-2 vaccine candidate

(PiCoVacc/CoronaVac) demonstrated those key findings that support the progression of PiCoVacc to clinical development:

- Strong immunogenicity with high levels of binding and neutralizing antibodies.
- Immune responses comparable or superior to those observed in convalescent human sera.
- Effective protection against viral challenge in rhesus macaques, with significant reduction in viral load and prevention of severe pulmonary pathology.
- Favorable safety profile with no evidence of systemic toxicity or adverse clinical findings

2- BBIBP-CorV Vaccine:

This study was conducted to evaluate the immunogenicity and protective efficacy of the inactivated SARS-CoV-2 vaccine candidate (BBIBP-CorV) across multiple animal models: BALB/c mice, Rats, Guinea pigs, Rabbits, Cynomolgus monkeys, and rhesus macaques" using Intramuscular (IM) and intraperitoneal (IP, mice) as Single-, two-, and three-dose schedules, Doses: 2, 4, and 8 µg/dose. The inactivated SARS-CoV-2 vaccine (BBIBP-CorV) demonstrated:

- Robust and consistent immunogenicity across multiple species.
- Dose and schedule dependent immune responses, with optimal efficacy in a three-dose regimen.
- Complete seroconversion in several animal models, 100% seroconversion by Day 21.
- Strong protective efficacy in rhesus macaques, with marked reduction or absence of viral replication.

3- NRC-VACC-101 (Egypt):

NRC-VACC-101 vaccine is an inactivated SARS-CoV-2 vaccine, consisting of purified viral particles diluted in phosphate-buffered saline (PBS) and Alum adjuvant. It has been developed by the Egyptian scientists at the National Research Centre, aiming to take part in the global effort to provide protection against the COVID-19 infection. The NRC-VACC-101 candidate vaccine was studied in animals through pre-clinical trials conducted on four different animal models with the objective of immunogenicity, protection, safety, and efficacy assessment of the vaccine.

Study Objective: To evaluate immunogenicity, safety, and protective efficacy in preclinical models, using escalating doses of viral antigen with alum adjuvant. Functional immunity was assessed by Viral Microneutralization (VMN) assay, and kinetics of antibody responses were monitored over 10 weeks.

Animal Models and Study Design:

Animal	N	Groups	Doses (µg/dose)	Route	Volume	Age/Weight	Control
Guinea pigs (female)	60	5	10, 20, 50, 100	IM	300 µL	6–8 wk, 280–300g	225 µL PBS + 75 µL alum

Mice (female, BALB/c)	60	5	3, 6, 15, 30	IM (2 sites)	100 µL	6–8 wk, 18–21g	75 µL PBS + 25 µL alum
Hamsters (female, Syrian)	60	5	3, 6, 15, 30	IM	300 µL	6–8 wk, 70–90g	225 µL PBS + 75 µL alum

Immunogenicity Results:

Guinea Pigs	• VMN titers <10 at baseline • Week 1: no statistical difference vs control • Weeks 2–7: statistically significant increases • Peak titer (10 µg group): 8.1 ± 0.45 • 20 µg group: peak 8.3 ± 0.71, sustained longer • 50 µg & 100 µg groups: rapid rise from week 2, remained high to week 10 (P<0.0001) • Differences between doses diminished by weeks 8–10 **Conclusion:** Even lowest dose induced at least 20-fold higher VMN titers than control.
Mice	• VMN titers <10 at baseline • Week 2: statistically significant increase in all vaccinated groups • Sustained high titers through week 10 (P<0.0001) • Dose-dependent trend observed, slight non-significant drop late in study **Conclusion:** NRC-VACC-101 induces rapid and sustained neutralizing antibody responses.
Hamsters	• VMN titers <10 at baseline • Week 2: significant rise begins • Week 3 onward: dose-dependent, statistically significant titers through week 10 • Week 3 titers (reciprocal values): o 3 µg: 4.3 ± 1 o 6 µg: 5.7 ± 1.3 o 15 µg: 6.3 ± 0 o 30 µg: 6.9 ± 0.89 (P≤0.01–0.0001) **Conclusion**: Robust neutralizing antibody responses observed in a dose-dependent manner.

➢ **Secondary Pharmacodynamics**

For CoronaVac, BBIBP-CorV and 3- NRC-VACC-101 the data only covered primary pharmacodynamics (immunogenicity and protective efficacy).

A. Pharmacokinetics and Drug Metabolism in Animals

There is **no conventional** pharmacokinetic ADME (absorption, distribution, metabolism, excretion) studies were performed. Only immunogenicity (VMN titers) was measured, which indirectly indicates systemic exposure to the antigen.

B. Toxicology and Safety Pharmacology

- **Single-dose toxicity:**

For BBIBP-CorV: Sprague-Dawley rats received 3× human-equivalent dose (24 µg) , showed that: No mortality, no clinical signs of toxicity, no changes in body weight, food intake, or histopathology.

For PiCoVacc: Acute administration well tolerated in mice and rats; no adverse effects reported.

For NRC-VACC-101:

1-Rats – NRC-VACC-101 Preclinical Safety Study:

Experimental Design:

Animals: 120 adult Wistar rats (60 males + 60 females), 140–160 g, 6–8 weeks old.

Groups: 5 groups (12 males + 12 females each):

- Control: vehicle (225 µL PBS + 75 µL alum)
- Vaccine: 3, 6, 15, 30 µg/dose, 300 µL total volume (225 µL PBS + 75 µL alum)

Study Duration: 6 weeks.

Endpoints Assessed: Mortality, body weight, food intake, clinical observations, body temperature, blood analysis, injection site reactions, histopathology.

Clinical Findings:

-No mortality observed.

-Body Weight & Food Intake: No significant differences for 3, 6, 15 µg; 50 and 30 µg doses caused temporary reductions, normalized later.

-Body Temperature: Slight increase on day 2 in females for 3 and 6 µg groups.

-Injection Site & Behaviour: No significant local reactions or behavioural changes observed.

-CBC & Biochemistry: No significant differences across all groups at any phase (RBCs, WBCs, platelets, hemoglobin, hematocrit, SGOT, SGPT, albumin, urea, creatinine, calcium).

-For Histopathology: the injection site showed mild, dose-dependent local inflammatory reaction, predominantly at 30 µg, Lymph nodes, thymus, spleen showed minimal changes at higher doses; otherwise, normal. Mild kidney degeneration in 30 µg; mild liver congestion; brain, reproductive organs unaffected.

Conclusion: Lower doses (3, 6, 15 µg) safe; highest dose (30 µg) has minor effects, avoid if possible.

2-Guinea Pigs – NRC-VACC-101 Preclinical Safety Study:

Experimental Design:

Animals: 60 adult female guinea pigs, 280–300 g, 6–8 weeks old.

Groups: 5 groups (n=12 each):

- Control: vehicle (225 µL PBS + 75 µL alum)
- Vaccine: 10, 20, 50, 100 µg/dose, 300 µL total (225 µL PBS + 75 µL alum)

Study Duration: 4 weeks.

Clinical Findings:

- No mortality observed.

-Body Weight:

10 & 20 µg: no significant change.

50 µg: transient reduction week 1, normalized later.

100: persistent reduction throughout 4 weeks (statistically significant).

-Food Intake:

10 & 20 µg: unaffected.

50 µg: reduced week 1, normalized later.

100 µg: reduced all 4 weeks (statistically significant).

-Behaviour & Injection Site: No notable changes.

-CBC & Biochemistry: No significant differences in RBC, WBC, haemoglobin, haematocrit, platelets, SGOT, SGPT, albumin, urea, creatinine, calcium, ferritin, D-dimer.

-For Histopathology: The injection site showed chronic local immune reaction (foamy histiocytic aggregates), Lymph nodes normal; follicular hyperplasia, scattered macrophages.

Lungs, spleen, kidney, brain, reproductive organs normal; mild liver vessel congestion.

Conclusion: Vaccine well tolerated at all doses, local chronic inflammation at injection site noted but no systemic organ toxicity.

****Overall preclinical safety Conclusion:** These preclinical safety studies conducted on two rodents i.e., rats and guinea pigs proved the overall good safety of the different doses of the inactivated vaccine both on the acute as well as the chronic state. There were no mortalities in any of the studied rodents for the length of the study. Besides all the available data obtained from the neurobehavioral, weight change, food intake, blood biochemistry and histological appearance of the vaccinated animals with the different doses ascertain the safety and well tolerability of the vaccine used in the study without any deleterious toxicological effect whether of short or long term. Furthermore, there was no notable blood profile nor blood chemistry changes of concern or any pathological derangement in the histological sections examined. This applies for both the

male and female rodents. Therefore, the safety of this vaccine warrants extension of this preclinical work to the human clinical trial with the appropriate doses.

- **Repeat-Dose Toxicity**

Preclinical Repeat-Dose Safety and Toxicology Evaluation of Inactivated NRC-VACC-01 Vaccine in Mice.

Toxicology Observations:

-Repeated IM administration of NRC-VACC-01 (6 µg/dose) well tolerated in mice.
-No systemic toxicity observed.
-Hematology, serum biochemistry, and coagulation parameters within normal limits.
-Histopathology confirms absence of organ-specific toxicity.
-Slight D-dimer elevation is transient and not associated with adverse effects.

Conclusion: The mice with a repeat dose of the vaccine showed no mortality or any significant change in their blood parameters and the gross and microscopic histological findings did not show any pathological deviation from the norm. The overall safety profile of the repeat dose of the inactivated vaccine was well acknowledged despite the high antibody titer that was maintained and persisted.

- **Genotoxicity:** No in vitro or in vivo genotoxicity assays were reported.
- **Carcinogenicity** No long-term carcinogenicity studies were performed in this preclinical study.
- **Immunotoxicity:** Safety endpoints included histopathology of immune organs (lymph nodes, thymus, spleen, Peyer's patches, bone marrow) with no pathological findings. D-dimer elevation observed is interpreted as transient inflammatory response, not immunotoxicity.
- **Immunogenicity:** VMN titers measured every 2 weeks; strong neutralizing antibody response after primary and booster doses.
  Peak titers at week 6: 1152 ± 286.2 ($P < 0.0001$ vs control).
  Titers remained elevated through week 14.
- **Local tolerance**: Injection site examined histologically; no tissue reaction or pathology observed.
- **Reproductive & developmental toxicity:** No studies in pregnant mice, fertility assessments, or embryo-fetal development were conducted.
- **Tissue cross-reactivity studies:** No studies assessing binding of vaccine antigen to normal tissues were reported.

- **Summary of previous clinical studies "**Literature Review of Data from Other Vaccines**":**

1-CoronaVac(formerly PiCoVacc Vaccine):

CoronaVac, developed by Sinovac Biotech, is an inactivated whole-virion SARS-CoV-2 vaccine indicated for active immunization against COVID-19 in adults aged ≥18 years. The vaccine received Emergency Use Listing (EUL) from the World Health Organization on 1 June 2021 and has since been authorized for emergency use in approximately 40 countries. Integrated clinical summary of CoronaVac (Sinovac) based on Phase 1/2 studies (Corona 01, Corona 02), Phase 3 trials (Corona 04, 06, 07), and supporting bridging study (Corona 05**)**

Objective: To evaluate the immunogenicity and safety of the inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy adults across different age groups.

Study Program and Vaccination Schedules:

Phase 1/2 Studies (China): Corona 01: Adults aged 18–59 years , and Corona 02: Adults ≥60 years

Bridging Study: Corona 05 (China)

Phase 3 Efficacy Trials: Corona 04: Brazil , Corona 06: Indonesia , and Corona 07: Turkey

Paediatric Study: Corona 03: Ages 3–17 years (not included in current evaluation).

CoronaVac is administered as a two-dose regimen. The evaluated schedules include:

Day 0 and Day 14 (emergency schedule)

Day 0 and Day 28 (routine schedule; associated with improved immunogenicity)

1. **Clinical Pharmacodynamics:**

CoronaVac is an inactivated SARS-CoV-2 vaccine formulated to elicit an humoral immune response. Following administration, the vaccine induces the production of neutralizing antibodies targeting viral antigens, thereby preventing viral entry into host cells and subsequent infection.

2. **Clinical Efficacy:**

A Phase 3 randomized controlled trial conducted in Brazil demonstrated a vaccine efficacy of **50.4%** against symptomatic COVID-19.

Post-authorization observational data from Chile demonstrated an effectiveness of approximately 67% in real-world settings.

These results indicate moderate protection against symptomatic infection, with improved effectiveness under programmatic use conditions.

3. **Clinical Safety:**

Phase 1 Studies

The incidence of adverse events (AEs) was: 29–38% in vaccine recipients (0,14 schedule) , 13–17% in vaccine recipients (0,28 schedule) , and 8–13% in placebo groups.

Phase 2 Studies

The incidence of AEs was: 33–35% in vaccine recipients (0,14 schedule) , 19% in vaccine recipients (0,28 schedule), and 18–22% in placebo groups.

Adverse events were predominantly mild to moderate in severity and transient in nature.

Lower reactogenicity was consistently observed with the longer dosing interval.

Post-Authorization Safety

Post-marketing pharmacovigilance data include: Approximately 35.8 million doses administered in China and approximately 20 million doses administered across Brazil, Indonesia, and Chile.

No unexpected safety signals were identified. The safety profile observed in real-world use is consistent with that established in clinical development.

4. **Immunogenicity:**

Phase 1 Clinical Trials

In healthy adults aged 18–59 years, seroconversion of neutralizing antibodies was observed:

At Day 14 following a 0 and 14-day schedule: 46–50% across dose groups

At Day 28 following a 0 and 28-day schedule: 79–83%

Phase 2 Clinical Trials

In expanded cohorts:

At Day 14 (0,14 schedule): 92–98% seroconversion

At Day 28 (0,28 schedule): 97–100% seroconversion

These findings demonstrate a dose-dependent and schedule-dependent immune response, with enhanced immunogenicity observed with extended dosing intervals.

2- BBIBP-CorV Vaccine, Sinopharm:

Objective: Evaluate immunogenicity, safety, and efficacy in adults.

Study Program and Vaccination Schedules:

Phase 1/2:Participants: 18–59 and ≥60 years

Doses: 2 µg, 4 µg, 8 µg; schedules 0,14; 0,21; 0,28 days

Neutralizing antibody titers:

Day 28: 169.5 (0,14), 282.7 (0,21), 218.0 (0,28)

Single dose (8 µg) lower (14.7)

Phase 3: Locations: UAE, Bahrain

Participants: 12,726 vaccine / 12,737 placebo

1. **Clinical Pharmacokinetics:**

There are no formal pharmacokinetic studies (ADME) have been conducted for BBIBP-CorV. Vaccine activity is assessed via: Neutralizing antibody responses (GMTs) and Seroconversion rates.
Pharmacokinetic evaluation is not required, as accepted by the World Health Organization and other regulatory authorities for inactivated vaccines.

2. Clinical Pharmacodynamics:

BBIBP-CorV is an **inactivated whole-virion SARS-CoV-2 vaccine** that induces an immune response through the generation of neutralizing antibodies against viral antigens, thereby preventing viral entry into host cells.

3. Clinical Efficacy:

Overall efficacy (Phase 3): 74% (against asymptomatic and symptomatic infection)
Efficacy against symptomatic infection: 78%
Efficacy against severe COVID-19: ~100%

4. Clinical Safety:

Phase 1 Clinical Safety

Adverse reactions within 7 days: 29% of vaccine recipients.
Most common systemic reaction: Fever (low incidence across dose groups).
Severity is mild to moderate.
No serious adverse events (SAEs) reported within 28 days.

Phase 2 Clinical Safety

Adverse reactions within 7 days: 23% of vaccine recipients.
Highest incidence observed in single-dose (8 µg) group.
Most reactions is mild to moderate.
One Grade 3 fever (placebo group), resolved without complications.

Overall Safety Assessment

Favourable tolerability profile.
No major safety concerns identified across studies
Lower reactogenicity observed with optimized two-dose regimens

5. Immunogenicity:

Phase 1 Findings:

Neutralizing antibody geometric mean titers (GMTs) at Day 42:

a. **Ages 18–59 years:**
   2 µg: 87.7

4 µg: 211.2
8 µg: 228.7

b. **Ages ≥60 years:**
2 µg: 80.7
4 µg: 131.5
8 µg: 170.9

Responses were **dose-dependent** and higher than placebo.

Phase 2 Findings:

Neutralizing antibody titers at Day 28:

4 µg (0,14): 169.5
4 µg (0,21): 282.7
4 µg (0,28): 218.0
8 µg single dose: 14.7

Two-dose regimens induced significantly higher immune responses than single-dose schedules.
Optimal immunogenicity observed with extended dosing intervals (0,21 or 0,28).

Safety Summary:

Vaccine	Preclinical	Clinical	Key Safety Findings
PiCoVacc	Mice, rats, macaques	–	Well tolerated, no toxicity, normal labs, mild lung pathology in challenge
BBIBP-CorV	Multiple animals	Phase 1–3	Well tolerated, high safety margin, no SAEs, mild/moderate reactions in humans
CoronaVac	–	Phase 1–3	Mild/moderate reactions, no SAEs, effective protection, post-marketing safety acceptable
NRC-VACC-101	Mice, hamsters, guinea pigs, rats	Phase 1 planned	Well tolerated, high immunogenicity, protective in challenge studies, no toxicity

- **Protocol:** Phase 1 Clinical Trial to Evaluate the Safety, Tolerability, and Immunogenicity of Inactivated SARS-CoV-2 Vaccine Against COVID-19 in Healthy Adults.

NRC-VACC-101 Vaccine is an inactivated SARS-CoV-2 vaccine was developed by the Egyptian National Research Centre in an attempt to provide an effective and safe vaccine for COVID-19.
The vaccine was prepared using ahCoV-19/Egypt/NRC-03/2020 SARS CoV?2 strain which was isolated in VeroE6 cells from an oropharyngeal swab specimen collected from a 34-year-old woman from El-Minya governate, Egypt. The isolation was previously investigated and a whole-genome comparison of the isolate

revealed more than 99.8% similarity to the reference 2019-nCoV WHUO1 and only five nucleotide mutations were detected in the isolate when compared with the reference 2019-nCov.

Phase: I

Objective(s):

Primary objectives	Secondary objectives
To evaluate the safety and tolerability of the proposed regimens of NRC-VACC-101 Vaccine in healthy population (for up to 28 days after the last vaccination dose) by assessing: • Reactogenicity profile of the NRC-VACC-101 Vaccine. • Solicited AE reported within 7 days and unsolicited AE within 28 days after each dose.	1.To evaluate the preliminary immunogenicity resulting from the proposed regimens of NRC-VACC-101 vaccine administration by assessing: • The seroconversion rate of neutralizing antibodies resulting from the NRC-VACC-101 Vaccine. • Cellular immunogenicity of the NRC-VACC-101 Vaccine. • Humoral immunogenicity of the NRC-VACC-101 Vaccine. 2. To recommend the dose level of NRC-VACC-101 Vaccine for the phase II trial.

Endpoint(s):

Primary Endpoint(s)	Secondary Endpoint(s)
1. Occurrence of Adverse events (AEs) or Serious adverse events (SAEs) throughout the study duration. 2. Immunogenicity index of neutralizing-antibody seroconversion rate tested by micro- neutralization assay in serum throughout the study duration.	**A. Safety:** 1. Nature and number of AEs for up to 28 days following the last dose of vaccination. 2. Occurrence of local reactogenicity signs and symptoms for up to 7 days following each vaccination. (pain, erythema, and swelling) 3. Occurrence of systemic reactogenicity signs and symptoms for up to 7 days following each vaccination. 4. Occurrence of abnormal changes in laboratory safety examinations baseline (hemoglobin, WBCs, platelets, ALT, AST, total bilirubin, creatinine, creatine phosphokinase, urine protein, urine sugar, urinary erythrocytes, and D-dimer). **B. Cellular and Humoral Immunogenicity:** 5. from The seroconversion rate of neutralizing antibodies (NAb) against SARS-COV-2 tested by

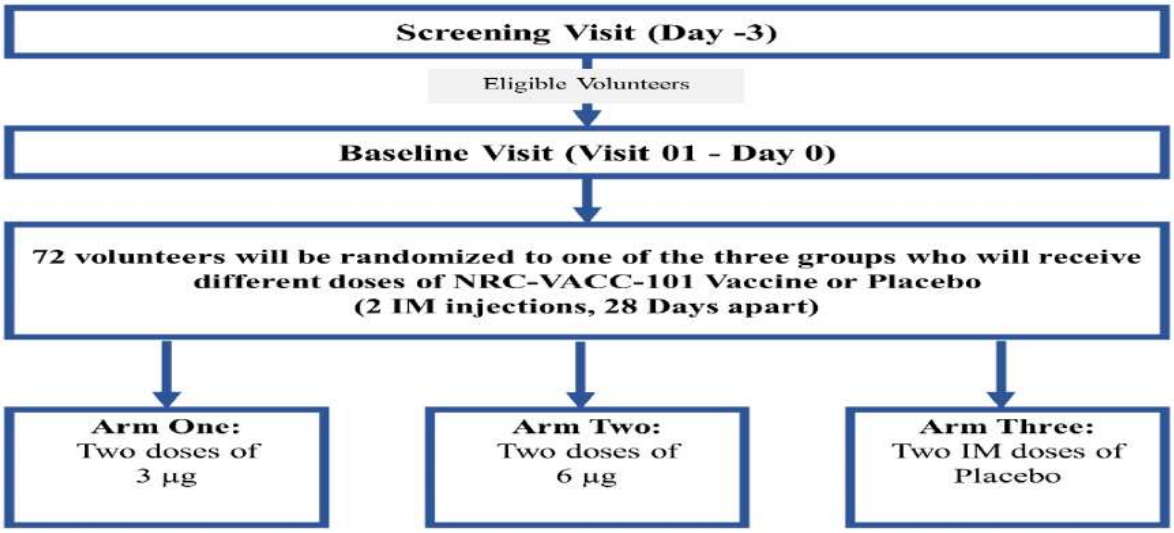
	micro-neutralization assay in serum (on days 07, 28, 35, and 56) compared to baseline. 6. Immunogenicity index of IgG antibody titer (on days 07, 28, 35, and 56, by serum ELISA) compared to baseline. 7. Immunogenicity index of IgM antibody seropositivity rate (on days 07, 28, 35, and 56, by serum ELISA) compared to baseline. 8. Immunogenicity index of Geometric mean titer (GMT) of neutralizing-antibody serum (on days 07, 8, 35, and 56, by micro-neutralization assay in serum) compared to baseline. 9. Immunogenicity index of Geometric mean ratio (GMR) of neutralizing antibody (on days 07, 28,35, and 56, by micro-neutralization assay in serum divided by the baseline titer) compared baseline. 10. Cell-mediated responses: -Levels of IL-1, 6, and 10, measured by ELISA on days 07, 28, 35, and 56 compared to baseline. -Levels of TNF-a measured by ELISA on days 28 and 56 compared to baseline. -Human Interferon-gamma (IFN-y) measured by ELISA (on days 28 and 56 compared to baseline) after Stimulation of proliferated peripheral blood mononuclear cells (PBMCs) with SARS-CoV-2 virus. -Percentages of CD3+CD4+ (T-helper) and CD3+CD8+ (T-cytotoxic) lymphocytes will be measured using flowcytometry on days 07, 28, 35, and 56 compared to baseline.

Rationale:

In this phase 1 study, the inactivated virus vaccine NRC-VACC-101 will be investigated for its safety and immunogenicity in healthy volunteers with the aim of providing effective and safe protection against COVID-19.

Design:

-This is a Phase I, Randomized, Open-Label Clinical trial.



-Eligible volunteers will be randomized in a **1:1:1** allocation ratio, into one of the **three study arms.** Volunteers will be randomized into one of the following arms to receive different doses of the Inactivated SARS-COV-2 Vaccine "NRC-VACC-101" as an IM Injection or Placebo:

Arm One:	**Arm Two:**	**Arm Three (Control arm):**
Volunteers will receive two IM doses of the vaccine, concentrations of 3 mcg, 28 days apart.	Volunteers will receive two IM doses of the vaccine, concentrations of 6 mcg, 28 days apart.	Volunteers will receive two IM doses of the placebo, 28 days apart.

-The first nine subjects will be initially vaccinated with their first dose, as per their assigned study arm determined by the randomization procedures and will be followed up until day 14 (visit 03). At this point in the study, the DSMB will review safety data before proceeding with vaccinating the rest of the recruited subjects.

-Eligible screened subjects will receive the first dose of vaccination (Arms 01 and 02) or placebo (Arm 03), at the baseline visit (any day from day -3 to day 0) once all data for inclusion/exclusion criteria are available (including laboratory reports) and the 2°¢ dose of vaccination in Arm 01 and 02, or placebo in Arm 03, on Visit 05 (Day 28).

Duration of study participation:

An estimated recruitment period of one month, an estimated vaccination period of 28 days (two IM

injections at a 28-day interval (Day 0 and Day 28), and an estimated follow-up period of one month from the second dose of vaccination/placebo.

A total of nine visits, following the screening visit, will be performed as shown in the table below. The visit window for the study visits will be +2 days.

Screening Visit	Visit 01 (First dose)	Visit 02	Visit 03	Visit 04	Visit 05 (Second dose)	Visit 06	Visit 07	Visit 08	Visit 09
Day -3	Day 0 ± 2 days	Day 07 ± 2 days	Day 14 ± 2 days	Day 21 ± 2 days	Day 28 ± 2 days	Day 35 ± 2 days	Day 42 ± 2 days	Day 49 ± 2 days	Day 56 ± 2 days

- ***Recommendation &/ or* Questions & Answers:** NA

- **Abbreviation:**

-**ADME**: Absorption, Distribution, Metabolism, Excretion
-**AE**: Adverse Event
-**BBIBP-CorV:** Beijing Bio-Institute Biological Products - Coronavirus Vaccine
-**CBC:** Complete Blood Count
-**COVID-19**: Coronavirus Disease 2019
-**D-dimer**: Degradation product of cross-linked fibrin
-**DSMB:** Data Safety Monitoring Board
-**EDA:** Egyptian Drug Authority
-**EUL:** Emergency Use Listing
-**GMT**: Geometric Mean Titer
-**IB:** Investigator's Brochure
-**IM**: Intramuscular
-**IMP**: Investigational Medicinal Product
-**IP:** Intraperitoneal
-**IWRS:** Interactive Web Response
-**NRC:** National Research Centre
-**NRC-VACC-101**: National Research Centre Vaccine Candidate 101
-**PBS:** Phosphate Buffered Saline
-**PD**: Pharmacodynamics

-**PI:** Principal Investigator
-**PK**: Pharmacokinetics
-**RBC**: Red Blood Cells
-**RCT**: Randomized Controlled Trial
-**SAE:** Serious Adverse Event
-**SARS-CoV-2**: Severe Acute Respiratory Syndrome Coronavirus 2
-**SGOT**: Serum Glutamic-Oxaloacetic Transaminase
-**SGPT:** Serum Glutamic-Pyruvic Transaminase
-**VMN**: Viral Microneutralization
-**WBC:** White Blood Cells
-**WHO:** World Health Organization