# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

10 Jun 2026

# A randomized, double-blinded, placebo-controlled phase I clinical trial to evaluate the safety and immunogenicity of three dose regimens of COVID-19 RBD protein recombinant vaccine (AmitisGen; 80µg and 120µg) in a healthy population

## Protocol summary

**Study aim**

To determine the safety and immunogenicity of COVID-19 recombinant RBD protein vaccine in a healthy population

**Design**

Phase I, randomized, double-blind, parallel arms, placebo-control clinical trial on 70 healthy volunteers

**Settings and conduct**

This double-blind (participants and outcome assessors) placebo control study will be conducted on 70 healthy volunteers. After random assignment to 80 micrograms, 120 micrograms, or placebo group, they will receive the intervention three times on days 0, 21, 35 and following-up until day 49 for any adverse events and measuring humoral and cellular immunity. All participants will be followed up for 360 days.

**Participants/Inclusion and exclusion criteria**

Main inclusion criteria: Healthy 18-50 years, willing to participate, the ability to understand the study, signing the informed consent, not being pregnant, using effective contraception during the study. Main exclusion criteria: Positive PCR test, previous history of infection (positive antibody), symptoms consistent with COVID-19, history of close contact with COVID-19 patient in the last 14 days, abnormal paraclinical findings, history of allergy to the vaccine, neurologic disease, immunodeficiency, coagulopathy, psychiatric and other chronic diseases, Receiving live vaccine in one month or other vaccines in 14 days before inoculation, Receiving immunoglobulins or blood products in 3 months before inoculation or investigational products in 6 months before inoculation, willing to pregnancy or lactation, the high-risk job for SARS-CoV2 exposure

**Intervention groups**

Group 1: 80 µg (30), Group 2: 120µg (30), Placebo (10)

**Main outcome variables**

Incidence of any side effects after injection, during 7 days, 125 days, and a year. The titer of specific antibodies (including spike, RBD, Neutralizing, ...), the incidence of SARS-COV-2 infection, measurement of cellular immunity.

## General information

**Reason for update**

**Acronym**

**IRCT registration information**

IRCT registration number: **IRCT20210620051639N1**
Registration date: **2021-06-25, 1400/04/04**
Registration timing: **registered_while_recruiting**

Last update: **2021-06-25, 1400/04/04**
Update count: **0**

**Registration date**

2021-06-25, 1400/04/04

**Registrant information**

**Name**
Jafar Salimian
**Name of organization / entity**
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Iran (Islamic Republic of)
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**Recruitment status**

**Recruitment complete**

**Funding source**

**Expected recruitment start date**

2021-06-25, 1400/04/04

**Expected recruitment end date**
2021-08-26, 1400/06/04
**Actual recruitment start date**
empty
**Actual recruitment end date**
empty
**Trial completion date**
empty

**Scientific title**
A randomized, double-blinded, placebo-controlled phase I clinical trial to evaluate the safety and immunogenicity of three dose regimens of COVID-19 RBD protein recombinant vaccine (AmitisGen; 80µg and 120µg) in a healthy population

**Public title**
Safety and immunogenicity of COVID-19 RBD protein recombinant vaccine (AmitisGen): phase I study.
**Purpose**
Prevention
**Inclusion/Exclusion criteria**
**Inclusion criteria:**
Age between 18 and 50 years old Healthy in terms of past medical history, physical examination, and laboratory data- Body mass index: 17-35 kg/m2 Willingness to participate in the study and complete follow-up Ability to comprehend study methodology Ability to comprehend and sign informed consent- Provision of consent to access medical documents in case of contracting COVID-19 For women: negative pregnancy screening Acceptance of contraception use from 21 days before randomization until six months after receiving the last vaccine dose Acceptance of not receiving blood product or bone marrow from randomization until three months after receiving last vaccine dose
**Exclusion criteria:**
Positive COVID-19 PCR test Positive antibodies against SARS-CoV-2 (IgG, IgM) History of infection with SARS-CoV-2 documented with RT-PCR test Close contact with COVID-19 infected individual in the past 14 days Isolation due to signs and symptoms that are suspicious of COVID-19 Fever (axillary temperature > 37° C), dry cough, fatigue, nasal congestion, rhinorrhea, sore throat, myalgia, diarrhea, dyspnea in the past 14 days Laboratory abnormalities in biochemistry profile, blood, and urine (including urea, creatinine, fasting blood sugar, Na, K, aspartate transaminase, alanine transaminase, alkaline phosphatase, total bilirubin, hemoglobin, leukocyte count, neutrophil count, lymphocyte count, platelet count, urine protein, urine glucose, blood cells in urine) History of severe allergic reactions or allergy to vaccine components (latex) Experience to severe allergic or allergic reactions to components of the recombinant RBD protein vaccine (latex sensitivity) Personal or family history of seizure, epilepsy, encephalopathy, psychiatric disorder Congenital malformations -History of neurologic diseases or seizure (except for febrile seizure at childhood) Growth disorders Genetic disorders Malnutrition Renal or liver abnormalities Uncontrolled hypertension (>140/90 mmHg) Heart failure with NYHA class ≥2 Recent exacerbations of cardiovascular disease include cardiovascular intervention, the addition of new cardiovascular drugs to control symptoms, or unstable angina. Chronic obstructive lung disease with GOLD score ≥2- Asthma Diabetic complications BMI > 35 kg/m2 History of malignancy in the past five years Exacerbation of chronic diseases in the past 7 days Immunodeficiency, lymphoma, leukemia, autoimmune diseases Thyroid disease or history of thyroidectomy without proper control Splenectomy or history of resection of solid organs Coagulation abnormalities Anti-tuberculosis treatment Positive HBSAg Positive HIV Ab Positive HCV Ab Receiving immunosuppressive therapy for 14 consecutive days in the past 3 months or need for such therapy in the following 6 months Receiving any off-label or investigational therapy for COVID-19 Receiving flu vaccine in the past 14 days or other vaccines in the past 4 weeks History of drug or alcohol abuse in the prior year Receiving immunoglobulin or blood products in the prior 3 months Receiving investigational drugs in the past 45 days Planning to receive other vaccines in the next month Severe psychiatric disorders interfering with participation in the trial Women with positive beta-HCG, pregnancy, or during breastfeeding, or plan to become pregnant during the study High risk occupation for COVID-19 exposure (health care workers) or with decision of investigators First degree family members of the trial personnel Any other reason that the investigators document making volunteers ineligible-
**Age**
From **18 years** old to **50 years** old
**Gender**
Both

**Phase**
1
**Groups that have been masked**

- Participant
- Care provider
- Investigator
- Outcome assessor

**Sample size**
Target sample size: **70**
**Randomization (investigator's opinion)**
Randomized
**Randomization description**
A random sequence of length 70 (the size of the sample size) is generated by the online system (SealedEnvelope.com). For this purpose, 10 random blocks with size 7 are produced, in each block, 3 people are given the low-dose vaccine, 3 people are given high-dose vaccine and 1 person is assigned to the placebo group. The generated codes are pasted on the vaccine vials before the start of the study and are assigned to the candidates during the study by the study software.
**Blinding (investigator's opinion)**
Double blinded
**Blinding description**
Each vaccine dose is in a separate vial with an identifier code. Vaccine boxes and vials are identical in shape, color, and smell, making participants, investigators, and outcome adjudicators all blinded to the randomized

intervention. After injection of each vaccine, the abbreviated ID of the participant and the date will be written on the outside box and a label with the same ID will be added to the trial file. Study personnel who are in charge of vaccine injection check all relevant IDs before injection. During the study, all vaccine packages will be archived.

**Placebo**
Used

**Assignment**
Parallel

**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**

**Name of ethics committee**
Reserch ethics committees of national research committee

**Street address**
13th floor, Block A, Ministry of health, Simaye Iran street, Shahrake ghods

**City**
Tehran

**Province**
Tehran

**Postal code**
1417993337

**Approval date**
2021-06-23, 1400/04/02

**Ethics committee reference number**
IR.NREC.1400.004

## Health conditions studied

### 1

**Description of health condition studied**
COVID-19

**ICD-10 code**
U07.1

**ICD-10 code description**
COVID-19, virus identified

## Primary outcomes

### 1

**Description**
Any immediate adverse reaction after inoculation

**Timepoint**
30 min after injection

**Method of measurement**
close monitoring

### 2

**Description**
Any local adverse events

**Timepoint**
0-7 days after each injection

**Method of measurement**
Examination, history, and report of the study participant based on the Vaccine Adverse Event Reporting System

### 3

**Description**
Any systemic adverse events

**Timepoint**
0-7 days after each injection

**Method of measurement**
Examination, history, and report of the study participant based on the Vaccine Adverse Event Reporting System

### 4

**Description**
Any laboratory adverse events

**Timepoint**
0-7 days after each injection

**Method of measurement**
Examination, history, and report of the study participant based on the Vaccine Adverse Event Reporting System

### 5

**Description**
Any serious adverse events

**Timepoint**
0-7 days after each injection

**Method of measurement**
Examination, history, and report of the study participant based on the Vaccine Adverse Event Reporting System

### 6

**Description**
Any serious adverse event, medically attended adverse event, or adverse event of interest

**Timepoint**
0-125 days after each injection

**Method of measurement**
Examination, history, and report of the study participant based on the Vaccine Adverse Event Reporting System

## Secondary outcomes

### 1

**Description**
IgG antibody against RBD protein

**Timepoint**
in days 0, 7, 28, 35, 42, and 49 after injection of the first dose

**Method of measurement**
based on geometric means and seroconversion (at least fourfold increase in antibody titer)

**2**

**Description**
IgG antibody level against RBD protein
**Timepoint**
in days 0, 7, 28, 35, 42, and 49 after injection of the first dose
**Method of measurement**
based on ELISA method and seroconversion rate (proportion of individuals with at least twofold and fourfold inreases) and seroresponse (proportion of individuals with an increase above the 95th percentile of placebo group titers)

**3**

**Description**
neutralizing antibodies
**Timepoint**
in days 0, 7, 28, 35, 42, and 49 after injection of the first dose
**Method of measurement**
based on geometric mean titers and ratios and seroconversion rate (proportion of individuals with at least twofold and fourfold inreases) and seroresponse (proportion of individuals with an increase above the 95th percentile of placebo group titers)

**4**

**Description**
Cellular immunity response
**Timepoint**
in days 0, 7, 28, 35, 42, and 49 after injection of the first dose
**Method of measurement**
determining Th1 or Th2 dominance based on levels of IL-4، IL-10، IL-12، IL-13 و INFγ with ELISA measurement, and levels of CD3، CD4، CD8 with INFγ based on flow cytometry measurement

## Intervention groups

**1**

**Description**
Intervention group: receiving 80 micrograms of RBD protein recombinant SARS-CoV-2 vaccine in days 0, 21, and 35; intramuscular (deltoid muscle)
**Category**
Prevention

**2**

**Description**
Intervention group: receiving 120 micrograms of RBD protein recombinant SARS-CoV-2 vaccine in days 0, 21, and 35; intramuscular (deltoid muscle)
**Category**
Prevention

**3**

**Description**
Control group: the placebo group will receive an intramuscular injection (in the deltoid muscle) consisting of buffer and adjuvant only, on days 0, 21, and 35
**Category**
Placebo

## Recruitment centers

**1**

**Recruitment center**
**Name of recruitment center**
Ŝhahid Ghassem Soleimani Clinical Trial Center
**Full name of responsible person**
Dr. Hassan Abolghasemi
**Street address**
Ŝhahid Ghassem Soleimani Clinical Trial Center, Baqiyatallah University of Medical Sciences,Shahid Nosrati Alley, Sŏuth Sheykh Bahaei, Mollasadra Street , Tehran,
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1435916471
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H.abolghasemi.ha@gmail.com

## Sponsors / Funding sources

**1**

**Sponsor**
**Name of organization / entity**
Bagheiat-allah University of Medical Sciences
**Full name of responsible person**
Dr. Jafar Salimian
**Street address**
Shahid Soleimani clinical trial center,Shahid Nosrati alley, Mollasadra st, Sheikh Bahaei st.
**City**
Tehran
**Province**
Tehran
**Postal code**
1435915371
**Phone**
+98 21 8216 2440
**Email**
jafar.salimian@gmail.com
**Grant name**
**Grant code / Reference number**
**Is the source of funding the same sponsor organization/entity?**
Yes
**Title of funding source**

Bagheiat-allah University of Medical Sciences

**Proportion provided by this source**

100

**Public or private sector**

Public

**Domestic or foreign origin**

Domestic

**Category of foreign source of funding**

*empty*

**Country of origin**

**Type of organization providing the funding**

Academic

## Person responsible for general inquiries

**Contact**

**Name of organization / entity**

Bagheiat-allah University of Medical Sciences

**Full name of responsible person**

Dr. Hassan Abolghasemi

**Position**

Professor

**Latest degree**

Subspecialist

**Other areas of specialty/work**

Pediatric Hematology and Oncology

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Baqiyatallah University of Medical Sciences, Shahid Nosrati alley, Shiekh Bahaei st., Mollasadra st,

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H.abolghasemi.ha@gmail.com

## Person responsible for scientific inquiries

**Contact**

**Name of organization / entity**

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**Full name of responsible person**

Dr. Hassan Abolghasemi

**Position**

Professor

**Latest degree**

Specialist

**Other areas of specialty/work**

Pediatric Hematology and Oncology

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## Person responsible for updating data

**Contact**

**Name of organization / entity**

Bagheiat-allah University of Medical Sciences

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Dr. Hassan Abolghasemi

**Position**

Professor

**Latest degree**

Subspecialist

**Other areas of specialty/work**

Pediatric Hematology and Oncology

**Street address**

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## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**

No - There is not a plan to make this available

**Justification/reason for indecision/not sharing IPD**

No plans to release patient data

**Study Protocol**

Yes - There is a plan to make this available

**Statistical Analysis Plan**

Yes - There is a plan to make this available

**Informed Consent Form**

Yes - There is a plan to make this available

**Clinical Study Report**

Yes - There is a plan to make this available

**Analytic Code**

Yes - There is a plan to make this available

**Data Dictionary**

Yes - There is a plan to make this available

**Title and more details about the data/document**

Data will be available to regulatory bodies and the ethics committee

**When the data will become available and for how long**

The protocol and results will become available to the public after completion of the study.

**To whom data/document is available**

The regulatory body and the ethics committee will have access to the study data. The monitoring team will have access to the study data during the conduct. DSMB will

have access to the study data and results in predefined timelines and decides about the continuation of the study.

**Under which criteria data/document could be used**

With the permission of the sponsor and the approval of regulatory

**From where data/document is obtainable**

The study sponsor is responding to this request

**What processes are involved for a request to access data/document**

After contacting the principal investigator and obtaining permission from the sponsor

**Comments**