

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

04 Oct 2023

### **A double-blinded, randomized, placebo-controlled Phase I Clinical trial to evaluate the safety and immunogenicity of COVID-19 inactivated vaccine (Shif-Pharmed) in a healthy population**

#### **Protocol summary**

##### **Study aim**

To determine the safety and immunogenicity of COVID-19 inactivated vaccine in a healthy population

##### **Design**

Phase I, randomized, double-blind, parallel arms, placebo-control clinical trial on 56 healthy volunteers

##### **Settings and conduct**

This double-blind (volunteers and outcome assessors) placebo control study will be conducted on 56 healthy volunteers at Eram Hotel in Tehran. After random assignment to 3 micrograms, 5 micrograms, or placebo group (based on two stages random allocation), they will receive the intervention twice on days 0 and 14 and following-up until day 28 for any adverse events and measuring humoral and cellular immunity. All participants will be followed up for 360 days to identifying any potential late side effects.

##### **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: 3 µg antigen protein (24), Group 2: 5 µg antigen protein (24), Placebo (8)

##### **Main outcome variables**

The occurrence of adverse events, Seroconversion rate, Neutralizing antibody, incidence of SARS-COV-2 infection, cytokines assay, Lymphocyte count

#### **General information**

##### **Reason for update**

##### **Acronym**

##### **IRCT registration information**

IRCT registration number: **IRCT20201202049567N1**

Registration date: **2020-12-15, 1399/09/25**

Registration timing: **prospective**

Last update: **2020-12-15, 1399/09/25**

Update count: **0**

##### **Registration date**

2020-12-15, 1399/09/25

##### **Registrant information**

##### **Name**

Mohammadreza Hosseinpour

##### **Name of organization / entity**

Shifa Pharmed Industrial Co

##### **Country**

Iran (Islamic Republic of)

##### **Phone**

+98 21 9109 0245

##### **Email address**

mr.hosseinpour@shifapharmed.com

##### **Recruitment status**

**Recruitment complete**

##### **Funding source**

##### **Expected recruitment start date**

2020-12-21, 1399/10/01

##### **Expected recruitment end date**

2021-02-18, 1399/11/30

**Actual recruitment start date**

empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

A double-blinded, randomized, placebo-controlled Phase I Clinical trial to evaluate the safety and immunogenicity of COVID-19 inactivated vaccine (Shif-Pharmed) in a healthy population

**Public title**

Phase 1 clinical trial of an inactivated COVID-19 vaccine (Shifa-Pharmed) in healthy individuals

**Purpose**

Prevention

**Inclusion/Exclusion criteria****Inclusion criteria:**

Aged 18 to 50 years Healthy general condition according to medical history and initial medical examinations Willing and able to cooperate throughout the study period according to the study protocol Being able to fully understand the study processes and understand the explanations of the facilitators correctly Being able to understand the contents of the informed consent form and sign it before entering the study Allowing researchers access to medical records, test results if hospitalized due to suspicion, or approval of COVID-19 A negative pregnancy test at screening or vaccination (women only) Using effective methods of contraception during the study (male and female) Volunteers who agree not to donate blood, blood products, or bone marrow from the start of the vaccine until three months after receiving the last dose

**Exclusion criteria:**

Confirmed, suspected, or asymptomatic COVID-19 detected by PCR at baseline. COVID-19 positive antibody History of SARS-CoV-2 infection History of contact with a person with SARS-CoV-2 infection (positive PCR test) during the last 14 days People in the home quarantine period due to Covid (suspicion of exposure or suspicious symptoms) Fever (axillary temperature greater than 37 ° C) Dry cough, extreme tiredness, nasal congestion, runny nose, sore throat, muscle aches, diarrhea, dyspnea, and shortness of breath during the 14 days prior to vaccination Abnormality in biochemistry, blood and urine laboratory tests History of severe allergy or allergic reactions to Inactivated vaccine components Personal or family history of seizure, epilepsy, encephalopathy or mental disorders Congenital malformations History of neurologic disorders or seizure or Guillain-Barre syndrome (excluding childhood febrile seizure) Growth disorders Any Genetic disorder History or signs of malnutrition Hepatorenal diseases Uncontrolled hypertension Diabetes complications BMI > 40 Any malignancy Acute diseases or an exacerbation of a chronic disease in the last 7 days Known case of immunodeficiency, HIV, lymphoma, leukemia, or other autoimmune diseases Thyroid disease or history of thyroidectomy Splenectomy or history of any organ removal History of coagulopathy Receiving Anti-TB

treatment Positive HBSAg Positive HIV test Positive HCV antibody Receiving immunomodulators or immunosuppressors at least 14 days in the past 3 months Receiving live vaccine in one month or other vaccines in 14 days before inoculation History of drug or alcohol abuse Receiving immunoglobulins or blood products in 3 months before inoculation Receiving any other investigational drug in 6 months before inoculation Planning to receive any vaccination in on month after inoculation History of severe mental disorders affecting the participation in the study Pregnant or lactating women or those who intend to become pregnant during the study period Having a high-risk job of being exposed to the SARS-CoV-2 virus or having a high risk of exposure according to the investigator evaluation Any other condition that makes a person inappropriate for participation based on the investigator opinion

**Age**From **18 years** old to **50 years** old**Gender**

Both

**Phase**

1

**Groups that have been masked**

- Participant
- Investigator
- Outcome assessor

**Sample size**Target sample size: **56****Randomization (investigator's opinion)**

Randomized

**Randomization description**

A two-stage individual permuted block randomization is planned for the study. At the first stage, 14 participants randomly receive a low dose of 3 micrograms (12 candidates) or placebo (2 volunteers). For this purpose, two random block sequences with size 7 are produced, including 6 vaccines and one placebo code. After getting approval for the safety of the low-dose vaccine, in the second stage, 42 volunteers are randomly assigned to the intervention group of 3 micrograms (12 participants), 5 micrograms (24 participants), and the placebo (6 participants). For this purpose, 6 blocks with size 7 (2 people in the group of 3 micrograms, 4 people in the group of 5 micrograms, one person in the placebo group) will be generated. All random allocation processes will be performed by an interactive web response system (IWRS).

**Blinding (investigator's opinion)**

Double blinded

**Blinding description**

Every dose of vaccine is packaged separately and has a unique identification number. Vials and boxes of vaccine and placebo have a similar shape and packaging that results in blinding for participants, investigators, and outcome assessors.

**Placebo**

Used

**Assignment**

Parallel

## Other design features

The Data and Safety Monitoring Board (DSMB) oversees the safety of participants throughout the study. The committee consists of seven independent members (including infectious disease specialist, immunologist, virologist, epidemiologist, vaccinologist, etc.). The DSMB is held at intervals of 7 days after the recruitment of first 3, 7, 14, 21 volunteers and then 14 days after the enrolment of 35th and 28 days after the 56th participant. The safety profile of the candidates is reviewed individually and the result of the committee is submitted to the regulatory body. The progress of the trial to next stage occurs only with the DSMB approval and the national regulatory authorities.

## Secondary Ids

empty

## Ethics committees

### 1

#### Ethics committee

##### Name of ethics committee

National research ethics committee

##### Street address

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

##### City

Tehran

##### Province

Tehran

##### Postal code

1417993337

#### Approval date

2020-12-02, 1399/09/12

#### Ethics committee reference number

IR.NREC.1399.003

## Health conditions studied

### 1

#### Description of health condition studied

COVID-19 disease

#### ICD-10 code

U07.1

#### ICD-10 code description

COVID-19, virus identified

## Primary outcomes

### 1

#### Description

Any immediate reaction after inoculation

#### Timepoint

0-30 minute after inoculation

#### Method of measurement

Close observation

### 2

#### Description

Percentage of local reactions (pain, redness, swelling, ....in injection site)

#### Timepoint

Days 0 to 7 after each inoculation

#### Method of measurement

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

### 3

#### Description

Percentage of systemic events (fever, headache, chills, vomiting, diarrhea, fatigues, muscle pain, joint pain, ....)

#### Timepoint

Days 0 to 7 after each inoculation

#### Method of measurement

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

### 4

#### Description

Incidence of any adverse event (AE)

#### Timepoint

Days 0 to 7 after each inoculation

#### Method of measurement

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

### 5

#### Description

Incidence of any serious adverse event (SAE)

#### Timepoint

Days 0 to 7 after each inoculation

#### Method of measurement

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

## Secondary outcomes

### 1

#### Description

Any adverse events (AEs or SAEs)

#### Timepoint

From Days 7 to 28 after inoculation

#### Method of measurement

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

### 2

#### Description

Percentage of seroconversion occurrence

#### Timepoint

Days 0, 7, 14, 21, 28, 90, 180, 360

#### Method of measurement

At least a 4-fold increase in antibody titer (IgG and IgM) above baseline : ELISA assay

### 3

**Description**

Antibody- IgG and IgM titer (The geometric mean titer of antibody)

**Timepoint**

Days 0, 7, 14, 21, 28 and 90, 180, 360 (follow up period)

**Method of measurement**

ELISA

### 4

**Description**

Neutralizing antibody activity

**Timepoint**

Days 0, 7, 14, 21, 28 and 90, 180, 360 (follow up period)

**Method of measurement**

ELISA

### 5

**Description**

Lymphocytes subset count (Including CD3+, 4+, 8+, NK cell, B cell, ...)

**Timepoint**

Days 0, 14 and 28 after inoculation

**Method of measurement**

Flow Cytometry

### 6

**Description**

Cytokine assay (including IL 1, 2,4,5,6,8,10,12,17A,17F,21IFN- gamma, TNF - alpha)

**Timepoint**

Days 0, 14 and 28 after inoculation

**Method of measurement**

ELISA

### 7

**Description**

The severity of SARS-COV-2 infection (if present)

**Timepoint**

Any time after inoculation: days 0 to 28

**Method of measurement**

Clinical grading

## Intervention groups

### 1

**Description**

Intervention group 1: 3 micrograms of antigen protein (Shifa Pharmed Co.) on days 0 and 14, which is received intramuscularly (deltoid muscle).

**Category**

Prevention

### 2

**Description**

Intervention group 2: 5 micrograms of antigen protein

(Shifa Pharmed Co.) on days 0 and 14, which is received intramuscularly (deltoid muscle).

**Category**

Prevention

### 3

**Description**

Control group: The placebo group will receive only aluminum hydroxide adjuvant in the form of deltoid intramuscular injection on days 0 and 14. Placebo is similar to the active vaccine in shape and volume.

**Category**

Placebo

## Recruitment centers

### 1

**Recruitment center****Name of recruitment center**

Eram Hotel

**Full name of responsible person**

Minoo Mohraz- Mohamadreza Salehi- Payam Tabarsi

**Street address**

Near West Hemmat Highway- Haghani Highway- Vanak square

**City**

Tehran

**Province**

Tehran

**Postal code**

1417993337

**Phone**

+98 21 2226 6644

**Email**

info@tehraneramhotel.com

**Web page address**

<http://tehraneramhotel.com/home-page/>

### 2

**Recruitment center****Name of recruitment center**

Imam Khomeini hospital, Infectious diseases clinic

**Full name of responsible person**

Minoo Mohraz- Mohamadreza Salehi- Payam Tabarsi

**Street address**

Imam Khomeini hospital complex, Gharib street

**City**

Tehran

**Province**

Tehran

**Postal code**

1419733141

**Phone**

+98 21 6119 3011

**Email**

Imamhospital@tums.ac.ir

**Web page address**

<http://ikhc.tums.ac.ir>

## Sponsors / Funding sources

### 1

#### Sponsor

**Name of organization / entity**

Shifa Pharmed Industrial Co.

**Full name of responsible person**

Mohammadreza Hosseinpour

**Street address**

Soha St., Shifa St.,Mapna Blv

**City**

Kordan

**Province**

Alborz

**Postal code**

1417993337

**Phone**

+98 21 9109 0245

**Email**

mr.hosseinpour@shifapharmed.com

**Web page address**

<https://en.bpharmed.com/>

**Grant name****Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

**Title of funding source**

Shifa Pharmed Industrial Co.

**Proportion provided by this source**

100

**Public or private sector**

Private

**Domestic or foreign origin**

Domestic

**Category of foreign source of funding**

empty

**Country of origin****Type of organization providing the funding**

Industry

## Person responsible for general inquiries

#### Contact

**Name of organization / entity**

Shifa Pharmed Industrial Co.

**Full name of responsible person**

Mohammadreza Hosseinpour

**Position**

Managing Director

**Latest degree**

Ph.D.

**Other areas of specialty/work**

Medical Pharmacy

**Street address**

Soha St., Shifa St.,Mapna Blv

**City**

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**Province**

Alborz

**Postal code**

1417993337

**Phone**

+98 21 9109 0245

**Fax****Email**

mr.hosseinpour@shifapharmed.com

**Web page address**

<https://en.bpharmed.com/>

## Person responsible for scientific inquiries

#### Contact

**Name of organization / entity**

Tehran University of Medical Sciences

**Full name of responsible person**

Minoo Mohraz

**Position**

Professor

**Latest degree**

Specialist

**Other areas of specialty/work**

Infectious diseases

**Street address**

AIDS research center, Tehran University of Medical Sciences

**City**

Tehran

**Province**

Tehran

**Postal code**

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**Email**

minoomohraz@gmail.com

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<https://ircha.tums.ac.ir/>

## Person responsible for updating data

#### Contact

**Name of organization / entity**

Tehran University of Medical Sciences

**Full name of responsible person**

Kazem Heidari

**Position**

Epidemiologist

**Latest degree**

Ph.D.

**Other areas of specialty/work**

Epidemiology

**Street address**

Unit 23, 4th floor, No. 1547, North Kargar Street

**City**

Tehran

**Province**

Tehran

**Postal code**

1417993337

**Phone**

+98 21 8896 3546

**Email**

k\_heidari@razi.tums.ac.ir

**Web page address**

http://ctc.tums.ac.ir

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

Undecided - It is not yet known if there will be a plan to make this available

**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**

Not applicable

**Data Dictionary**

Not applicable

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

Participants' data will be available for regulatory and ethics committee for decisions.

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

Documents including study protocol and the results will be available to the public after the study ends.

**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**