# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

07 Nov 2026

## A double-blind, randomized, placebo-controlled Phase II/III Clinical trial to evaluate the safety and efficacy of COVID-19 inactivated vaccine (Shifa-Pharmed) in a population aged 18 to 75 years

## Protocol summary

**Study aim**
To determine the efficacy and immunogenicity of COVID-19 inactivated vaccine (Shifa-pharmed)

**Design**
Phase 2/3, randomized, double-blind, parallel arms, placebo-controlled clinical trial on 20000 volunteers

**Settings and conduct**
This double-blind (volunteers and outcome assessors) placebo-controlled trial will be conducted on 280 healthy volunteers in phase 2 at Eram Hotel in Tehran. In phase 3, 20000 volunteers in six cities will be included. After random assignment to 5 micrograms or placebo group, they will receive the intervention twice on days 0 and 28 and be followed up for efficacy, immunogenicity, any adverse events, and COVID-19 incidence.

**Participants/Inclusion and exclusion criteria**
Main inclusion criteria: Healthy 18-75 years, willing to participate, the ability to understand the study, signing the informed consent, using effective contraception during the study. Main exclusion criteria: Positive PCR test, previous history of infection (positive antibody) in phase 2, symptoms consistent with COVID-19, history of close contact with COVID-19 patient in the last 14 days, history of allergy to the vaccine, immunodeficiency, coagulopathy, severe 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, History of recent travel abroad.

**Intervention groups**
5 µg antigen protein (28 days of doses interval), placebo groups ( 28 days of doses interval)

**Main outcome variables**
Vaccine efficacy in prevention of COVID-19 incidence, severe disease, and COVID-19 related death, immunogenicity, and adverse events

## General information

**Reason for update**

**Acronym**

**IRCT registration information**
IRCT registration number: **IRCT20201202049567N3**
Registration date: **2021-03-13, 1399/12/23**
Registration timing: **prospective**

Last update: **2021-03-13, 1399/12/23**
Update count: **0**

**Registration date**
2021-03-13, 1399/12/23

**Registrant information**

**Name**
Mohammadreza Hosseinpour

**Name of organization / entity**
Shifa Pharmed Industrial Co

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Iran (Islamic Republic of)

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**Recruitment status**
**Recruitment complete**

**Funding source**

**Expected recruitment start date**
2021-03-14, 1399/12/24

**Expected recruitment end date**
2021-05-21, 1400/02/31

**Actual recruitment start date**
empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

A double-blind, randomized, placebo-controlled Phase II/III Clinical trial to evaluate the safety and efficacy of COVID-19 inactivated vaccine (Shifa-Pharmed) in a population aged 18 to 75 years

**Public title**

Evaluate the safety and efficacy of COVID-19 inactivated vaccine

**Purpose**

Prevention

**Inclusion/Exclusion criteria**

**Inclusion criteria:**

Aged 18 to 75 years Being able to fully understand the study processes and understand the explanations of the facilitators correctly 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 the researchers to access medical records and test results if hospitalized due to suspected, or confirmed COVID-19 Using effective methods of contraception during the study at least two months after the second dose of vaccine Volunteers who agree not to donate blood, blood products, or bone marrow from the start of the vaccine until 21 days after receiving the last dose of the vaccine

**Exclusion criteria:**

Confirmed, suspected, or asymptomatic COVID-19 detected by PCR at baseline History of contact with a person with SARS-CoV-2 infection (positive PCR test) during the last 14 days History of SARS-CoV-2 infection (Only in immunogenicity subsample Fever or at least two of these symptoms: Dry cough, severe fatigue, nasal congestion, runny nose, sore throat, myalgia, diarrhea, dyspnea, and shortness of breath during the 14 days prior to vaccination History of severe allergic reaction to vaccination or allergic reactions to Inactivated vaccine components Known case of tuberculosis, hepatitis B or hepatitis C History of coagulopathy History of splenectomy Uncontrolled hypertension, uncontrolled diabetes, uncontrolled chronic cardiac, renal, neurologic, or severe pulmonary disease Acute diseases or an exacerbation of a chronic disease in the last 7 days Any malignancy, immunodeficiency, HIV, lymphoma, leukemia, or other autoimmune diseases Receiving immunomodulators or immunosuppressors at least 14 days in the past 3 months or planning to use in the next year Receiving live vaccine in one month or other vaccines in 14 days before inoculation History of drug or alcohol abuse in the last 12 months caused medical, familial or occupational problems Receiving immunoglobulins or blood products in 3 months before inoculation or planning to use in the next year Receiving any other investigational drug in 6 months before inoculation Having a plan to participate in a drug trial during the study period 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 History of travel abroad in the last 14 days Any other condition that makes a person inappropriate for participation based on the investigator opinion

**Age**

From **18 years** old to **75 years** old

**Gender**

Both

**Phase**

2-3

**Groups that have been masked**

- Participant
- Care provider
- Investigator
- Outcome assessor

**Sample size**

Target sample size: **20000**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

Phase 2: For less than 50 years participants, a randomized list with a length of 200 will be produced. Each sequence has a ratio of 4:1 vaccine to placebo and 160 participants will receive the active vaccine and 40 participants will receive a placebo. Sequences are generated using sealedenvelope.com by the block size of 5 (40 blocks) which has four interventions and one placebo in each block. For 51 to 75 years participants, the randomization sequence will be separately generated for 80 participants (64 active intervention and 16 placeboes) in a similar way. Phase 3: in this stage, stratified block randomization will be performed based on six cities and two age groups (<50 years and 51-75 years). Each stratum consists of blocks of size of 3 and a ratio of 2:1 (vaccine to placebo). 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**

## 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**
2021-03-10, 1399/12/20
**Ethics committee reference number**
IR.NREC.1399.008

## 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**
Vaccine efficacy of Shifa-pharmed inactivated SARS-COV-2 vaccine
**Timepoint**
14 to 180 days after the last dose of intervention
**Method of measurement**
Comparing confirmed COVID-19 cases

**2**

**Description**
Neutralizing antibody (phase 2)
**Timepoint**
Day 0 of vaccination and 14, 28, 42, 90,180 and 360 days after the second dose
**Method of measurement**
Virus neutralization test

**3**

**Description**
Anti SARS-COV-2 antibody titer (IgG, IgM) (Geometric mean titer) (phase 2)
**Timepoint**
Day 0 of vaccination and 14, 28, 42, 90,180 and 360 days after the second dose
**Method of measurement**
ELISA

**4**

**Description**
Severe COVID-19 cases
**Timepoint**
Days 14 to 180 after second dose
**Method of measurement**
Comparing confirmed severe COVID-19 cases

## Secondary outcomes

**1**

**Description**
Vaccine efficacy of Shifa-pharmed inactivated SARS-COV-2 vaccine
**Timepoint**
From 181 to 360 days after receiving the last dose of intervention
**Method of measurement**
comparing confirmed COVID-19 case

**2**

**Description**
Severe COVID-19 cases
**Timepoint**
181 to 360 days after second dose
**Method of measurement**
Comparing confirmed severe COVID-19 cases

**3**

**Description**
Any immediate reaction after inoculation
**Timepoint**
0-30 minute after inoculation
**Method of measurement**
Close observation

**4**

**Description**
Local reactions (pain, redness, swelling, ....) in injection site
**Timepoint**
Days 0 to 28 after each inoculation
**Method of measurement**
Examination, history, and report of the study participant based on the Vaccine Adverse Event Reporting System

**5**

**Description**
Systemic events (fever, headache, chills, vomiting, diarrhea, fatigues, muscle pain, joint pain, ....)
**Timepoint**
Days 0 to 28 after each inoculation
**Method of measurement**
Examination, history, and report of the study participant based on the Vaccine Adverse Event Reporting System

**6**

**Description**
Occurrence of any serious adverse event
**Timepoint**
Days 0 to day 360 after second dose
**Method of measurement**
Examination, history, and report of the study participant based on the Vaccine Adverse Event Reporting System

**7**

**Description**
Single dose efficacy of Shifa-pharmed inactivated SARS-COV-2 vaccine
**Timepoint**
day 1 after first doe to second dose
**Method of measurement**
Confirmed COVID-19 cases

## Intervention groups

**1**

**Description**
Intervention group 2: 5 micrograms of antigen protein (Shifa Pharmed Co.) on days 0 and 28, which is received intramuscularly (deltoid muscle).
**Category**
Prevention

**2**

**Description**
Control group: The placebo group will receive only aluminum hydroxide adjuvant in the form of deltoid intramuscular injection on days 0 and 28. 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
**Fax**
**Email**
lkafami@gmail.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**
تهران
**Province**
Tehran
**Postal code**
1419733141
**Phone**
+98 21 6119 3011
**Email**
Imamhospital@tums.ac.ir
**Web page address**
http://ikhc.tums.ac.ir

**3**

**Recruitment center**
**Name of recruitment center**
Selected 16-hour COVID-19 center in Tehran
**Full name of responsible person**
Minoo Mohraz
**Street address**
Tehran
**City**
Tehran
**Province**
Tehran
**Postal code**
1417993337
**Phone**
+98 21 9109 0245
**Email**
minoomohraz@gmail.com

**4**

**Recruitment center**
**Name of recruitment center**
Selected 16-hour COVID-19 center in Karaj
**Full name of responsible person**
Mojtaba Hedayat Yaghoobi
**Street address**
Karaj
**City**
تهران
**Province**
Alborz
**Postal code**
1417993337
**Phone**
+98 21 9109 0245

**Email**
minoomohraz@gmail.com

**5**

**Recruitment center**
**Name of recruitment center**
Selected 16-hour COVID-19 center in Mashhad
**Full name of responsible person**
Rosita Khodashahi
**Street address**
Mashhad
**City**
Mashhad
**Province**
Razavi Khorasan
**Postal code**
1417993337
**Phone**
+98 21 9109 0245
**Email**
rkhodashahi@yahoo.com

**6**

**Recruitment center**
**Name of recruitment center**
Selected 16-hour COVID-19 center in Shiraz
**Full name of responsible person**
Mohsen Moghadami
**Street address**
Shiraz
**City**
Shiraz
**Province**
Fars
**Postal code**
1417993337
**Phone**
+98 21 9109 0245
**Email**
moghadami@sums.ac.ir

**7**

**Recruitment center**
**Name of recruitment center**
Selected 16-hour COVID-19 center in Isfahan
**Full name of responsible person**
Farzin Khorvash
**Street address**
Isfahan
**City**
Isfahan
**Province**
Isfehan
**Postal code**
1417993337
**Phone**
+98 21 9109 0245
**Email**
khorvash@med.mui.ac.ir

**8**

**Recruitment center**
**Name of recruitment center**
Selected 16-hour COVID-19 center in Booshehr
**Full name of responsible person**
Katayoon Vahdat
**Street address**
Bushehr
**City**
Bushehr
**Province**
Boushehr
**Postal code**
1417993337
**Phone**
+98 21 9109 0245
**Email**
vahdatk@gmail.com

## 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**
Kordan

**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**
1417993337

**Phone**
+98 21 6658 1583

**Email**
minoomohraz@gmail.com

**Web page address**
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

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**Province**
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**Postal code**
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**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**