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Study to test the non-inferiority of the inactivated trivalent influenza vaccine adjuvanted with IB160 from Instituto Butantan compared to a high-dose inactivated trivalent influenza vaccine in adults aged 60 years and older

Submission date 13/11/2025	**Recruitment status** Not yet recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [X] Record updated in last year
Registration date 21/11/2025	**Overall study status** Ongoing	
Last Edited 21/11/2025	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims

Influenza is a significant public health concern in Brazil, especially among the elderly and those with chronic conditions. In 2022, there were over 37,000 hospitalizations and more than 3,200 deaths attributed to the flu, with the majority of deaths occurring in those over 60. This unpublished protocol (FLA-01-IB), phase 3, randomized, double blind (Participant; Investigator; Sponsor) study aims to investigate the non-inferiority, safety and immunogenicity of a trivalent influenza vaccine (fragmented, inactivated) adjuvanted with IB160 (VII3a-IB) towards the registered high-dose trivalent influenza vaccine (VII-HD), 21 days after one dose (0,5mL) of a intramuscular vaccination, in healthy individuals aged 60 years or older. Besides, the consistency (immunogenicity) of three different lots of vaccine (VII3a-IB), produced consecutively, is going to be assessed for guaranteeing the good practices in the manufacturing process.

Who can participate?

6900 participants coming from the ordinary population will be invited to compose the total study sample.

What does the study involve?

Study outcomes include immunogenicity (soroprotection and seroconversion using blood samples) using the Hemagglutinin and the Microneutralization tests as bases for calculation of the Geometric Mean Ratio (GMT) of each vaccine strain in both vaccines pre and postvaccination in the target population. The reason of GMTs (rGMT)> 2/3, for all the strains, between both vaccines, assuming a confidence interval inferior limit (CI) of 95% is the criteria to show the non-inferiority between the adjuvanted Butantan trivalent vaccine and the High Dose comparator. Lot equivalency is demonstrated when the 95% CI limits of the rGMTs of the strains present in

each of the three batches of VII3a-IB (rGMTsBatches 1/2, rGMTsBatches 1/3 and rGMTsBatches 2 /3) were between 2/3 and 3/2 for all comparisons and strains. Safety is assessed by adverse events collection, which after a causality relationship analysis; reveal the adverse reactions of each vaccine during six months. Morevover, serious adverse events and adverse events of special interest will be listed for both vaccines. Safety is supervised by an independent Data and Safety Monitoring Board. Screening, medical examination and randomization are based on inclusion and exclusion criteria, assessed after the signature of the Consent Inform Form (in accordance with this protocol, Good Clinical Practice (GCP/ICH E6 [R3]), the Declaration of Helsinki, and applicable regulatory requirements).

What are the possible benefits and risks of participating?
Risks include allergy to the vaccine products (egg proteins) and infection in the administration site. They will be minimized by ensuring that blood collections are performed by qualified and trained professionals in accordance with the study's standard operating procedures for blood collection. Benefits include the protection of vulnerable people to influenza-related complications (elderly) and the possibility of free vaccination with the VII-HD vaccine, already registered in Brazil but not yet included in the National Immunization Program, which has proven to have a better immune response and efficacy compared to the standard non-adjuvanted influenza vaccine.

Where is the study run from?
Instituto Butantan (Brazil)

When is the study starting and how long is it expected to run for?
February 2026 for approximately 6 months.

Who is funding the study?
This study is financially supported by Fundação Butantan (Brazil)

Who is the main contact?
Fernanda Castro Boulos, MD, PhD, Medical Director of Centro de Ensaios Clínicos and Farmacovigilância, Instituto Butantan, located at Avenida Vital Brazil, 1500 - Butantã, São Paulo, 05503-900, Brazil.

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Additional identifiers

Protocol serial number
FLA-01-IB

Study information

Scientific Title
A randomized, double-blind, parallel-group, multicenter Phase III clinical trial to evaluate the immunogenicity, safety, and lot consistency of the IB160-adjuvanted inactivated trivalent influenza vaccine and its non-inferiority compared to a high-dose inactivated trivalent influenza vaccine in adults 60 years of age and older

Acronym
FLA-01-IB

Study objectives
Co-primary immunogenicity objectives:
1. To show that the immunogenicity of the trivalent influenza vaccine (fragmented, inactivated) adjuvanted with IB160 (VII3a-IB) is non-inferior to that of the high-dose trivalent influenza vaccine (fragmented, inactivated) (VII-HD), 21 days after vaccination, in individuals aged 60 years or older.
2. To show that the immunogenicity of VII3a-IB, 21 days after vaccination, is equivalent across three consecutively produced batches.

Primary safety objective:
1. To evaluate the safety profile of VII3a-IB and VII-HD up to seven days after vaccination in individuals aged 60 years or older.
Secondary immunogenicity objective:
2. To show that the immunogenicity of VII3a-IB is superior to that of VII-HD, 21 days after vaccination, in individuals aged 60 years or older.

Secondary safety objective:
1. To evaluate the safety profile of VII3a-IB and VII-HD throughout the entire study participation period in individuals aged 60 years or older.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 03/11/2025, Faculdade De Medicina De São Jose Do Rio Preto - FAMERP (Avenida Brigadeiro Faria Lima, n° 5416, bloco FAEPE, térreo, Sala 2, São José do Rio Preto - SP, 15090000, Brazil; +55 (17)3201-5813; cepfamerp@famerp.br), ref: 7.944.853

Study design
Phase III non-inferiority randomized double-blind parallel-group multicenter study with an active comparator

Primary study design
Interventional

Study type(s)
Efficacy, Prevention, Safety

Health condition(s) or problem(s) studied
Influenza

Interventions
The safety and non-inferiority (rGMT) in terms of immunogenicity (HI antibodies titers and seroconversion, assessed for every vaccine strain) of VII3a-IB compared to VII-HD, 21 days after vaccination, in individuals aged 60 years or older, randomized into two groups, receiving a single shot (0.5 ml) of each vaccine.

Participants will be randomized 1:1 to receive either VII3a-IB or VII-HD using Interactive Response Technology (IRT). Randomization will be stratified by research center and age.

Intervention Type
Biological/Vaccine

Phase
Phase III

Drug/device/biological/vaccine name(s)
Trivalent Influenza Vaccine (Fragmented, Inactivated, Adjuvanted) from Instituto Butantan (VII3a-IB) and Trivalent Influenza Vaccine (Fragmented, Inactivated) High Dose (VII-HD)

Primary outcome(s)
1. Ratio of the geometric mean titers of HI antibodies induced by VII3a-IB compared to VII-HD, for A/H1N1, A/H3N2 and B/Victoria lineage strains, 21 days after vaccination.
2. Difference in seroconversion rates between VII3a-IB and VII-HD, measured through HI antibody titers, for A/H1N1, A/H3N2 and B/Victoria lineage strains, 21 days after vaccination.

Key secondary outcome(s))
1. Ratio of the geometric mean titers of HI antibodies induced by VII3a-IB compared to VII-HD, for A/H1N1, A/H3N2, and B/Victoria lineage strains, 21 days after vaccination.
2. Difference in seroconversion rates between VII3a-IB and VII-HD, measured through HI antibody titers, for A/H1N1, A/H3N2, and B/Victoria lineage strains, 21 days after vaccination.
3. Ratio of the geometric mean titers of HI antibodies induced by the VII3a-IB batches (batch1 /batch2, batch1/batch3, and batch2/batch3) for A/H1N1, A/H3N2, and B/Victoria lineage strains, 21 days after vaccination.
4. Frequency (n, %) of participants with solicited (local and systemic) and unsolicited adverse reactions occurring up to seven days after vaccination, for VII3a-IB and VII-HD.
5. Frequency (n) and intensity of solicited (local and systemic) and unsolicited adverse reactions occurring up to seven days after vaccination, for VII3a-IB and VII-HD.
6. Description of solicited adverse reactions occurring up to seven days after vaccination according to: medication use (%), duration and time to onset, for VII3a-IB and VII-HD.
7. Frequency (n, %) of participants with adverse events occurring throughout the entire study period, for VII3a-IB and VII-HD.
8. Frequency (n), intensity, causal relationship with the vaccine, and predictability of AEs occurring throughout the study participation period, by grade, for VII3a-IB and VII-HD.
9. Frequency (n, %) of participants with AEs occurring throughout the study participation period, for VII3a-IB and VII-HD.
10. Frequency (n), intensity, and causal relationship with the vaccine of AEs occurring throughout the study participation period, by grade, for VII3a-IB and VII-HD.
11. Description of solicited and unsolicited AEs occurring up to 21 days after vaccination according to: medication use (%) and duration and time to onset of the event, for VII3a-IB and VII-HD.
12. Description of unsolicited AEs occurring up to 21 days after vaccination according to: medication use (%) and duration and time to onset of the reaction, for VII3a-IB and VII-HD.

Completion date
01/03/2027

Eligibility

Key inclusion criteria
1. Adult aged 60 years or older at the time of signing the informed consent form
2. Able to understand the study aims, based on the Investigator's assessment, and agrees to follow all study procedures
3. Provision of free and informed written consent

Participant type(s)
Population

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
60 years

Upper age limit
99 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Participation in another clinical trial within 28 days prior to screening or having planned participation in another clinical trial during the study period.
2. Pre-existing health condition that is unstable, at the discretion of the study physician.
3. Pre-existing health condition that led to hospitalization within 90 days prior to study screening.
4. Dementia or any other cognitive condition at a stage that may interfere with adherence to the study protocol, at the discretion of the study physician.
5. Influenza vaccine: having been vaccinated with any influenza vaccine within 180 days prior to screening or having planned vaccination with another influenza vaccine, other than the study vaccine, during participation in the study.
6. Other vaccines (except influenza): having been vaccinated within 14 days prior to screening with any inactivated vaccine, or within 28 days prior to screening with any live attenuated vaccine, or having planned vaccination with any vaccine up to 21 days after the study vaccination.
7. Known hypersensitivity to egg proteins or any of the constituents of the study vaccines.
8. History of Guillain-Barré Syndrome or other demyelinating disease such as encephalomyelitis and transverse myelitis.
9. Thrombocytopenia or bleeding disorder that contraindicates intramuscular vaccination or phlebotomy for sample collection.
10. Continuous use, or use within seven days prior to screening, of anticoagulant medication (such as factor Xa inhibitors, direct thrombin inhibitors, warfarin, low molecular weight heparin, or fondaparinux) at a full anticoagulant dose.
11. Having received immunoglobulins, blood, or blood products within the last 180 days prior to

screening.
12. Altered immunocompetence (immunosuppression, immunodeficiency, or immunocompromise) primary or secondary due to:
12.1. Health condition (including, but not limited to, solid organ transplant, HIV, renal failure on hemodialysis, hepatic insufficiency with cirrhosis, heart failure grade III or IV according to the New York Heart Association classification29 and asplenia).
12.2. Active infectious disease or under treatment at screening (including, but not limited to, tuberculosis, pneumonia, osteomyelitis and endocarditis). Individuals with chronic hepatitis B or C, whether or not under treatment, may be included in the study.
12.3. Use of systemic corticosteroids (oral, intravenous or intramuscular) at a dose equivalent to ≥20 mg/day of prednisone for more than 14 days or a cumulative dose greater than 280 mg, in the last 90 days prior to screening. Topical, inhaled and intranasal corticosteroids are permitted. Intermittent use (one dose in the last 30 days prior to screening) of intra-articular corticosteroids is also permitted.
12.4. Having received an antineoplastic, immunosuppressant, immunomodulatory agent or radiotherapy in the last 180 days prior to screening.
13. Malignant neoplasm at the time of screening or a history of malignant neoplasm with less than five years of disease-free survival at the time of screening (with the exception of basal cell carcinoma of the skin, localized papillary thyroid cancer and localized prostate cancer under active surveillance).
14. Abuse of alcohol and/or illicit drugs in the last 12 months before screening that may compromise compliance with study procedures, at the discretion of the study physician. 15. Inability to obtain a blood sample for immunogenicity assessment at the Day 1 visit.
16. Being part of the study team, having a first-degree relative who is a member of the study team (parents, children, in-laws, stepchildren, sons-in-law and daughters-in-law), or living in the same household as a member of the study team.
17. Any other condition or circumstance that, in the opinion of the Investigator and/or the study physician, may increase the likelihood or severity of an unfavorable outcome due to participation in the study and interfere with adherence to the protocol or with the study results.

Date of first enrolment
01/03/2026

Date of final enrolment
01/08/2026

Locations

Countries of recruitment
Brazil

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Sponsor information

Organisation
Instituto Butantan

ROR
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Not defined

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Fundação Butantan

Alternative Name(s)
Butantan Foundation

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Brazil

Results and Publications

Individual participant data (IPD) sharing plan

Datasets generated in this study will be published as a supplement to the results publication. Details with José Moreira (jose.amoreira@fundacaobutantan.org.br).

IPD sharing plan summary

Published as a supplement to the results publication