

SOBERANA®02

VACCINE:	SOBERANA®02
COMPANY:	Finlay Vaccine Institute
CURRENT STATE:	Emergency Use Authorization for individuals over 19 years old Emergency Use Authorization for pediatric population from 2 to 18 years old
EFFICACY:	91,2% against symptomatic disease 75,7% against infection 100% against severe disease 100% against death

VACCINE CHARACTERISTICS:

1. DESCRIPTION

Preventive vaccine against COVID-19 diseases developed by Finlay Vaccine Institute in collaboration with Center for Molecular Immunology from the Biotechnological and Pharmaceutical Industries Group, BioCubaFarma. It is a protein subunit vaccine composed of SARS-CoV-2 Receptor Binding Domain (RBD) protein (sequence 319-541) produced by biotechnology in CHO cells, covalently conjugated to Tetanus Toxoid and absorbed in Aluminum Hydroxide gel. Each unit of Tetanus Toxoid contains between 4 and 8 units of the SARS-CoV-2 protein.

The platform on which the vaccine SOBERANA®02 is based, is well known, and predicts high safety with very few adverse events and a potential efficacy. In it lies one of its strengths, using a conjugation method used for more than 15 years in *Quimil-Hib*® (Conjugated vaccine against *Haemophilus Influenzae tipo b*) in the pediatric population. The Tetanus Toxoid has also been used as a carrier protein in other conjugated vaccines developed by Finlay Vaccine Institute as *Quimi-Vio*® (conjugated vaccine candidate against *Streptococcus Pneumoneae*).

2. ADVANTAGES

- Constitutes the first and the only conjugated vaccine in the existing vaccines against SARS-CoV-2 virus.
- Created on the basis of platforms known for their safety.
- Potential efficacy both infants and elderly population.
- Potential long-term immune response, due to the induction of T and B cell memories.
- It is covered by patent application.

3. MILESTONES

- Second Cuban and Latin-American vaccine candidate (the first one was SOBERANA®01) against SARS-CoV-2 virus, included in the World Health Organization Draft.
- First Cuban and Latin-American vaccine candidate against SARS-CoV-2 virus to start executing Phase I, Phase II and Phase III Clinical Trials.
- Used in the First Childhood Vaccination Campaign against Covid-19 worldwide.

4. CLINICAL TRIALS

Before starting the clinical evaluation phase, the vaccine was extensively evaluated in animal models demonstrating its non-toxicity and the ability to generate a high cellular response, including neutralizing antibodies. In addition, the induction of immunological memory of both B and T cells was observed.

The Phase I started in October 2020 and concluded in February 2021 included 40 apparently healthy subjects in an age range between 19 and 59 years old. Two Soberana®02 formulations (high and low) were evaluated in this trial. Both were safe and well tolerated, without the presence of serious and severe adverse events related to the vaccination. The immunogenicity results obtained with the highest doses support its selection as the formulation to continue with the following phases of clinical evaluation.

The Phase IIa/b initiated on December 2020 and currently ongoing included a total of 910 apparently healthy subjects in an age range between 19 and 80 years old. So far, all individuals included in phase IIa have received their complete vaccination scheme. Safety analyzes performed after each dose administered have shown that the candidate is safe and well tolerated, without the presence of serious and severe adverse events related to vaccination.

SOBERANA®02 concluded the Phase III Clinical Trial with excellent results. Started in March 8th, 2021 with the inclusion of 44,010 subjects, in Havana, Cuba. The volunteers received mainly two vaccination schemes, two-doses scheme with Soberana®02 and three-doses scheme with two doses of Soberana®02 and a booster dose of SOBERANA®Plus. It was about Phase III Clinical Trial, multicenter, adaptive, placebo-controlled, and double-blind in volunteers aged between 19 and 80 years old. Also was approved by National Regulatory Authority (CECMED), the execution of the interventional study in 150, 000 volunteers mainly workers from health and biopharmaceutical

sectors. This study initiated March 22th, 2021, in Havana, and it complements the Phase III Clinical Trials.

More information about the protocols of the aforementioned Clinical Trials can be found at the site: <https://rpcec.sld.cu/en/home>.

The results of the Phase II, showed that after completing the immunization scheme with Soberana Plus, 96, 6% of responding subjects were obtained. The demonstrated efficacy, with the heterologous three-doses scheme, was found to be 91, 2% against symptomatic disease, 75, 7% against infection, and 100% against symptomatic disease and death. This efficacy was reached in an complex scenario of different variants of strains with the predominance of the Beta strain (isolated in South Africa). This is the same scheme that is currently underway in a Phase I/II Clinical Trial in the pediatric population, showing high safety.

The Clinical Trial Phase I-II (named SOBERANA PEDIATRIA) in the pediatric population (Cuban children and adolescents) started on June 14th in 350 volunteers in the age range from 3 to 18 years old. It is an open-label, adaptive and multicenter study with a three-dose scheme. More information about the protocols of this trial can be found at the site: <https://rpcec.sld.cu/en/trials/RPCEC00000374-En>

The June 29th SOBERANA®02 received the Emergency Use Authorization in the Islamic Republic of Iran. The Regulatory Authority of that country, granted the authorization base on the recognition of the results of the pharmaceutical development of the product, the evidence of safety and immunogenicity demonstrated in the clinical trials of Phase I and II carried out in Cuba, as well as per the 62% clinical efficacy for two-dose scheme reported in the interim analysis of the Phase III Clinical Trial.

On August 20th, 2021, the Emergency Use Authorization of SOBERANA®02 in Cuba was issued by the Cuban Regulatory Authority CECMED after a rigorous evaluation process, when it was shown that it meets the requirements and parameters demanded in terms of quality, safety and effectiveness.

On September 3rd, 2021, CECMED issued the Emergency Use Authorization of SOBERANA®02 and SOBERANA®Plus in its heterologous scheme for the use in pediatric population from 2 to 18 years old, and this authorization allowed on September 5th start the First Childhood Vaccination Campaign against Covid-19 worldwide.

5. PUBLICATIONS

- Article published in **ACS Central Science** titled: **“SARS-CoV-2 RBD-Tetanus Toxoid Conjugate Vaccine Induces a Strong Neutralizing Immunity in Preclinical Studies”**, referred to the preclinical results of the vaccine SOBERANA®02. It can be accessed through the following link:

<https://pubs.acs.org/doi/pdf/10.1021/acscchembio.1c00272#>

- Article published in **ACS Central Science** titled: “**Molecular Aspects Concerning the Use of the SARS-CoV-2 Receptor Binding Domain as a Target for Preventive Vaccines**”. It can be accessed through the following link:

<https://pubs.acs.org/doi/10.1021/acscentsci.1c00216>

6. INDICATION

Prevent coronavirus disease (COVID-19) caused by the SARS-CoV-2 virus in apparently healthy individuals.

7. COMPOSITION

Each dose of SOBERANA[®]02 contains 25 micrograms of RBD protein conjugated to Tetanus Toxoid and absorbed in Aluminum Hydroxide gel.

8. PRESENTATION

Multi-dose (10 doses) vials and single-dose vial without thimerosal.

9. PHARMACEUTICAL FORM

Parenteral injectable (liquid) suspension.

10. DOSAGE

In clinical studies, schemes of two doses of SOBERANA[®]02 and three doses (including the third dose of SOBERANA[®]Plus) have been evaluated 28 days between each application.

11. PHYSICAL APPEARANCE

The vaccine SOBERANA[®]02 is a white opalescent suspension.

12. ROUTE OF ADMINISTRATION

Intramuscular

13. ADVERSE REACTIONS

In clinical studies, adverse reactions in participants over 19 years old have been rare,

predominantly mild intensity and locals, especially slight local pain at the injection site, mild general malaise, and no serious or severe adverse events related with the vaccination.

There were no serious adverse events consistent with vaccination. Only 13.8% of the individuals presented some adverse event. The most frequent adverse event was local pain at the injection site, representing 33.9% of the total reported events. Unlike that reported by other COVID vaccines, no cases of myocarditis, thromboembolic phenomena or Guillain Barré were observed during the duration of the study. This corresponds to the expected safety profile for the conjugate vaccine platform.

14. STORAGE CONDITIONS

The vaccine SOBERANA®02 is stored in a temperature between 2 and 8 °C. Stability studies are carried out to determine its life span.

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