# SOBERANA®Plus

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| **VACCINE:** | **SOBERANA®Plus** |
| **COMPANY:** | **Finlay Vaccine Institute** |
| **CURRENT STATE:** | **Emergency Use Authorization in its booster vaccine concept:**<br>- **Pediatric population (from 2 to 18 years old), applicated after two doses of SOBERANA®02 in a three-dose heterologous scheme.**<br>- **Individuals previously vaccinated with two doses of SOBERANA®02 in a three-dose heterologous scheme (over 19 years old).**<br>- **COVID-19 convalescent adults (over 19 years old) (a single dose)**<br>- **COVID-19 convalescent pediatric population (from 2 to 18 years old) (a single dose)** |
| **CONCEPTION:** | **Booster vaccine** |

## VACCINE CHARACTERISTICS:

### 1. DESCRIPTION

The vaccine SOBERANA®Plus has been conceived as a booster vaccine with the ability to reactive the pre-existing immune response and with potential protection from reinfection with the new strains, both in convalescent patients, previously exposed to the SARS-CoV-2 virus and in people immunized with another vaccine. This means that it can serve as a booster or combination of any other vaccine, with a single dose.

Preventive vaccine against COVID-19 disease created by Finlay Vaccine Institute in collaboration with the Center for Molecular Immunology from the Biotechnology 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 expressed in dimeric form and absorbed in gel of Aluminum Hydroxide.

The platform for obtaining recombinant proteins, on which the vaccine SOBERANA®Plus is based, is well known. The vaccine immunogens obtained by this route are characterized by their safety, low

reactogenicity and induction of a powerful immune response. An example of vaccines that this platform uses in Cuba is the preventive vaccine against Hepatitis B, Heberbiovac HB®, as well as the vaccine against lung cancer, based on the recombinant epidermal growth factor CIMAvax-EGF®.

## 2. ADVANTAGES

- It has a formulation capable of reactivating a pre-existing immune response either in an individual exposed to the SARS-CoV-2 virus (convalescent), or in individuals who have had a first vaccination scheme with another vaccine.
- Induces an important neutralizing response in convalescents after a single dose of SOBERANA®Plus.
- It has a high standard of safety.
- Potential booster vaccine for protection against mutant strains.
- Potential booster vaccine for population groups with high levels of risks, with serious morbidities.
- It is covered by patent application.

## 3. MAIN MILESTONE

- Used as a first vaccine as a booster dose in the First Childhood Vaccination Campaign against COVID-19 worldwide.
- SOBERANA®Plus constitutes the first COVID-19 vaccine officially authorized as a booster dose in a heterologous scheme in the world, for both adults and children.
- SOBERANA®Plus constitutes the first COVID-19 booster vaccine officially authorized in the world, for both the convalescent adults and convalescent children.

## 4. CLINICAL TRIALS

The vaccine SOBERANA®Plus found one of five formulations used in the Phase I Clinical Trials that began in August 2020. Based on the preliminary results obtained, SOBERANA®Plus was conceived as a booster vaccine, both for convalescents from COVID-19 and for individuals vaccinated with other formulations (Cuban vaccines SOBERANA®02 and SOBERANA®01)

The Phase I Clinical Trial of SOBERANA®Plus for convalescents in Havana, Cuba, concluded in March 2021 with very good results. It included 30 convalescent COVID-19 subjects in an age range between 19 and 59 years, to evaluate and test the vaccine`s ability to stimulate natural immunity with single dose.

The partial results obtained in Phase I mentioned were excellent. High safety and immunogenicity were demonstrated in convalescent subjects.

The SOBERANA®Plus Phase II Clinical Trial is concluded with the inclusion of 450 convalescents in the age range between 19 and 80 years old. Currently the data is being processing.

Also SOBERANA®Plus is included in the Phase II and III Clinical Trials (adults) and Phase I-II (pediatric population) of the other Cuban vaccine SOBERANA®02, as a booster dose in the three-dose scheme. The results of the efficacy in the Phase III (adults) with this heterologous three-dose scheme, was found to be 91, 2% against symptomatic disease, 75, 7% against infection, and 100% against symptomatic severe disease and death. This efficacy was reached in a complex scenario of different variants of strains with the predominance of the Beta strain (isolated in South Africa).

Was approved by National Regulatory Authority (CECMED), the execution of the interventional study in convalescents from Cuban health sector and subjects from BioCubaFarma. This study started in early June, 2021, and it complements the Phase II Clinical Trials in Covid-19 convalescent population.

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

On August 20th, 2021, the Emergency Use Authorization of SOBERANA®Plus in Cuba, as a booster dose applicated after two doses of SOBERANA®02 in an three-doses heterologous scheme, 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.

On September 23th, 2021, after a rigorous analysis, CECMED issued the Emergency Use Authorization of SOBERANA®Plus in the Covid-19 convalescent adults over 19 years old, with excellent clinical results.

On September 28th, 2021, CECMED issued its approval for the beginning of the clinical trial in convalescent pediatric population of range age from 2 to 18 years old.

On October 11, 2021, the results of the Phase III Clinical Trial developed at the Pasteur Institute of Iran on the efficacy of the heterologous scheme of SOBERANA®02 and SOBERANA®Plus were confirmed against a scenario where the Delta strain predominates (in July 71 , 9% and August 95.4%). This study included 24,000 subjects in an age range of 18 to 80 years. The interim analysis showed that the efficacy of the vaccine in preventing confirmed hospitalization for COVID-19 with two doses was 76.8% and in the three-dose regimen it was 91.7%.

On November 1st, 2021, the final efficacy results of the Phase III Clinical Trial of two doses of SOBERANA®02 were confirmed with of 71.0% against the circulating Beta and Delta strains. With the third dose of SOBERANA®Plus, the efficacy increased to 92.4%.

On September 28th, 2021, CECMED issued its approval for the start of the clinical trial in a convalescent pediatric population in the age range of 2 to 18 years.

On December 7th 2021, CECMED issued the Emergency Use Authorization of SOBERANA®Plus in the COVID-19 convalescent pediatric population from 2 to 18 years old, with very good results.

Work is underway to obtain the recombinant protein from new combinations of mutations in order to assemble it in the SOBERANA®Plus concept.

## 5. PUBLICATIONS

- Article published in **The Lancet Regional Health- Americas** titled: **"A single dose of SARS-CoV-2 FINLAY-FR-1A enhances neutralization response in Covid-19 convalescents, with a very good safety profile: An open-label phase 1 clinical trial"** referred to important results of the vaccine SOBERANA®Plus. It can be accessed through the following link:

https://www.thelancet.com/action/showPdf?pii=S2667-193X%2821%2900075-2

## 6. INDICATION

Reactive the pre-existing immune response in the individual exposed to the coronavirus disease (COVID-19) caused by the SARS-CoV-2 virus and in subjects who have had a primo-vaccination scheme with other vaccines.

## 7. COMPOSITION

Each dose contains 50 micrograms of RBD protein absorbed in Aluminum Hydroxide gel.

## 8. PRESENTATION

Single-dose vial without thimerosal.

## 9. PHARMACEUTICAL FORM

Parenteral injectable (liquid) suspension.

## 10. DOSAGE

The vaccine SOBERANA®Plus is administered intramuscularly with a single dose as a booster vaccine.

## 11. PHYSICAL APPEARANCE

The vaccine SOBERANA®Plus is a white opalescent suspension.

## 12. ROUTE OF ADMINISTRATION

Intramuscular

## 13. ADVERSE REACTIONS

In clinical studies, adverse reactions in participants between 19 and 80 years old have been rare, predominantly mild intensity and locals, especially slight local pain and redness in the injection site, mild general malaise, and no serious adverse event 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®Plus is stored in a temperature between 2 and 8 $^{o}$C. Stability studies are carried out to determine its life span.

## CONTACT PERSON

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