RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK FASE I
VAKSIN SARS-COV-2 AJUVAN ALUM
PRODUKSI PT. BIO FARMA

Informasi Umum

1. Vaksin SARS-CoV-2 adalah vaksin dengan platform subunit protein yang dikembangkan oleh PT. Bio Farma menggunakan *seed* vaksin dari *Baylor College of Medicine (BCM)*. Vaksin uji menggunakan ajuvan Alum.
2. Uji klinik fase I yang diajukan telah didukung oleh studi non klinik berupa studi toksisitas akut dan subkronik pada tikus dan kelinci dan studi imunogenisitas pada mencit. Selain itu, tersedia data uji non klinik dari BCM yaitu uji imunogenisitas dan uji tantang pada hewan mencit dan macaca.

Informasi Uji Klinik

1.	**Judul Protokol**	:	***A Phase I, Observer-Blind, Randomized, Controlled Study of the Safety and Immunogenicity of SARS-CoV-2 Protein Subunit Recombinant Vaccine in Healthy Populations Aged 18 Years and Above in Indonesia*** Versi 3.1 tanggal 24 November 2021
2.	**Produk Uji**	:	Vaksin SARS-CoV-2 0,5 ml (50 mcg protein rekombinan subunit Receptor Binding Domain (RBD) SARS-CoV-2 dan 200 µg aluminium as adjuvant), diberikan 3 kali secara intramuscular Produsen: PT. Bio Farma
3.	**Produk Pembanding**	:	Vaksin SARS-CoV-2 inactivated 600 SU (Coronavac) diberikan 2 kali secara intramuscular + 1 kali placebo Produsen Coronavac: Sinovac ; Produsen Placebo: PT. Bio Farma
4.	**Center / Peneliti**	:	Departemen Ilmu Kesehatan Anak, Fakultas Kedokteran Universitas Indonesia / Prof. Dr.dr. Rini Sekartini, SpA (K)
5.	**Sponsor**	:	PT. Bio Farma
6.	**Persetujuan Etik**	:	No. 845/UN2.F1/ETIK/PPM.00.02/2021 tanggal 6 September 2021 dari Komite Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Indonesia – RSUPN Dr. Cipto Mangunkusumo
7.	**Desain Uji Klinik**	:	*Observer-blind, randomized, controlled prospective intervention study*
8.	**Jumlah Subjek**	:	*60 subjects*
9.	**Tujuan Uji Klinik**	:	*Primary Objective:* *To evaluate the safety of the SARS-CoV-2 protein subunit recombinant vaccine within 7 days after each dose.* *Secondary Objective* - *To evaluate the safety of the SARS-CoV-2 protein subunit recombinant vaccine within 28 days after each dose.* - *To evaluate the preliminary immunogenicity profile of the SARS-CoV-2 protein subunit recombinant vaccine.* - *To compare safety evaluation between SARS-CoV-2 protein subunit recombinant vaccine and control group.*
10.	**Kriteria Eligibilitas**	:	**Kriteria Inklusi / *Inclusion criteria*** *1. Clinically healthy subjects within the following age groups: adults (18-59 years) and elderly (60 years and above.*

2. *Subjects have been informed properly regarding the study and signed the informed consent form*
3. *Subjects will commit to comply with the instructions of the investigator and the schedule of the trial.*

Kriteria Eksklusi / *Exclusion criteria*

1. *Subjects concomitantly enrolled or scheduled to be enrolled in another trial.*
2. *History of vaccination with any COVID-19 vaccine (based on anamnesis).*
3. *Subjects who have history of COVID-19 (based on anamnesis or other examinations).*
4. *Evolving mild, moderate or severe illness, especially infectious disease or fever (body temperature ≥37.5℃, measured with infrared thermometer/thermal gun).*
5. *The result of rapid antigen test is positive.*
6. *Women who are lactating, pregnant or planning to become pregnant during the study period (judged by self-report of subjects and urine pregnancy test results).*
7. *Abnormality hematology and biochemical test results (for main study subset).*
8. *History of asthma, history of allergy to vaccines or vaccine ingredients, and severe adverse reactions to vaccines, such as urticaria, dyspnea, and angioneurotic edema.*
9. *History of uncontrolled coagulopathy or blood disorders contraindicating intramuscular injection.*
10. *Patients with serious chronic diseases (serious cardiovascular diseases, uncontrolled hypertension and diabetes, liver and kidney diseases, malignant tumors, etc) which according to the investigator might interfere with the assessment of the trial objectives.*
11. *Subjects who have any history of confirmed or suspected immunosuppressive or immunodeficient state, or received in the previous 4 weeks a treatment likely to alter the immune response (intravenous immunoglobulins, blood-derived products or long-term corticosteroid therapy (> 2 weeks)).*
12. *Subjects who have history of uncontrolled epilepsy or other progressive neurological disorders, such as Guillain-Barre Syndrome.*
13. *Subjects receive any vaccination (other than COVID-19 vaccine) within 1 month before and after IP immunization.*
14. *Subjects plan to move from the study area before the end of study period.*

11. ***Endpoint*** : ***Primary Endpoints*:**
Number and percentage of subjects with solicited and unsolicited adverse events within 7 days after each dose

Secondary endpoints

Safety

- *Number and percentage of subjects with solicited and unsolicited adverse events within 28 days after each dose.*
- *Comparison of number and percentage of subjects with adverse events and serious adverse events between vaccine and active control group within 28 days after each dose.*
- *Any deviation from laboratory evaluation of SGOT/SGPT and Albumin that probably related to the dosing 28 days after the first dose for liver function evaluation.*
- *Any deviation from routine laboratory evaluation that probably related to the dosing 7 days after the whole schedule dose.*

Immunogenicity

- *Seropositive rate and GMT anti-RBD antibody IgG titer (ELISA) at baseline, day 28, 56, 84.*
- *Seroconversion of anti-RBD antibody IgG titer (ELISA) at day 28, 56, 84*
- *Seropositive rate and GMT of neutralizing antibody titer at baseline, day 28, 56, 84*
- *Seroconversion of neutralizing antibody titer at day 28, 56, 84*
- *Comparison of seropositive rate, seroconversion and GMT anti-RBD antibody IgG titer (ELISA) between two-dose and three-dose regimen of dosing.*
- *Comparison of seropositive rate, seroconversion and GMT of neutralizing antibody between two-dose and three dose regimen of dosing.*

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi terhadap protokol yang diajukan yang didukung oleh tim ahli melalui rapat pada tanggal 7 Agustus 2021 dengan hasil sebagai berikut:

1. Berdasarkan hasil uji non klinik pada mencit, tikus dan kelinci, vaksin dapat ditoleransi dengan baik dan menghasilkan respon imun antibodi dan meningkat seiring peningkatan dosis (25 mcg dan 50 mcg).
2. Desain uji klinik dengan membandingkan keamanan vaksin uji dan pembanding sebagai tujuan utama dapat diterima.
3. Vaksin uji klinik yang akan digunakan telah memenuhi persyaratan mutu.

Keputusan

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik No. RG.01.06.1.2.12.21.462 tanggal 6 Desember 2021