RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK FASE III
VAKSIN SARS-COV-2 AJUVAN ALUM + CYTOSINE-PHOSPHATE-GUANINE (CPG)
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 dan Cytosine-Phosphate-Guanine oligodeoxynucleotides (CpG)-1018.
2. Uji klinik fase 3 yang diajukan telah didukung oleh studi non klinik berupa studi toksisitas akut dan subkronik pada tikus dan kelinci dan studi imunogenisitas pada mencit dan Macaca serta data keamanan dan imunogenisitas uji klinik fase I dan II.

Informasi Uji Klinik

1.	**Judul Protokol**	:	***Immunogenicity & Safety of SARS-CoV-2 Protein Subunit Recombinant Vaccine (Bio Farma) Adjuvanted with Alum+CpG 1018 Compared to Registered Covid-19 Vaccine (Covovax – Protein Subunit Vaccine) in Healthy Populations Aged 18 Years and Above in Indonesia (Phase III)*** Versi 1.a dated 14 Mei 2022
2.	**Produk Uji**	:	Vaksin SARS-COV-2 0,5 mL (25 mcg protein rekombinan subunit *Receptor Binding Domain* (RBD) SARS-CoV-2 dan 750 mcg CpG 1018) diberikan 2 kali secara intramuskular Produsen: PT. Bio Farma
3.	**Produk Pembanding**	:	Covovax (5 µg SARS-CoV-2 protein *spike* rekombinan dengan adjuvan 50 µg Matrix-M) diberikan 2 kali secara intramuscular Produsen: Serum Institute of India
4.	**Center / Peneliti**	:	1. Departemen Ilmu Kesehatan Anak, Fakultas Kedokteran Universitas Indonesia / Prof. Dr. dr. Rini Sekartini, SpA (K) (Fase 3) 2. Fakultas Kedokteran Universitas Diponegoro, Semarang / dr. Yetty Movieta Nency, Sp.A.(K) 3. Fakultas Kedokteran Universitas Andalas / dr. Asrawati, M.Biomed, SpA(K) 4. Fakultas Kedokteran Universitas Hasanuddin / Dr. dr. Martira Maddeppungeng, Sp.A(K)
5.	**Sponsor**	:	PT. Bio Farma
6.	**Persetujuan Etik**	:	1. No. 729/UN.16.2/KEP-FK/2022 tanggal 17 Mei 2022 dari Komisi Etik Penelitian Fakultas Kedokteran Universitas Andalas. 2. No. 123/EC/KEPK/FK/UNDIP/IV/2022 tanggal 23 Mei 2022 dari Komisi Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Diponegoro.
7.	**Desain Uji Klinik**	:	*Main Study I, Exploratory Study Subset: Observer blind, randomized, active-controlled prospective intervention study* *Main Study II: Open-label, randomized study to evaluate safety*
8.	**Jumlah Subjek**	:	*4,050 subjects*
9.	**Tujuan Uji Klinik**	:	*Primary Objective* *To evaluate immunogenicity of SARS-CoV-2 Protein Subunit Recombinant Vaccine (Bio Farma)* *Secondary Objective* - *To evaluate safety of SARS-CoV-2 Protein Subunit Recombinant Vaccine (Bio Farma)*

- *To compare safety and immunogenicity between SARS-CoV-2 protein subunit recombinant vaccine (Bio Farma) and control group*
- *To evaluate safety and immunogenicity of lot-to lot consistency using three batches of the vaccine*
- *To evaluate antibody persistence at 3, 6 and 12 months after primary series*
- *Exploratory: to assess cellular immunity of the vaccine at 14 days, 6 months and 12 months after primary series (for Exploratory Study subset)*

10. Kriteria *Eligibilitas* **:**

Kriteria Inklusi / *Inclusion criteria*

1. *Clinically healthy subjects aged 18 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.*
3. *History of COVID-19 within 1 month (for mild moderate disease) or 3 months (for severe disease) prior to enrollment.*
4. *Evolving mild, moderate, or severe illness, especially infectious disease, or fever (body temperature ≥37.5℃, measured with infrared thermometer/thermal gun).*
5. *Women who are pregnant or planning to become pregnant during the study period (judged by self report of subjects and urine pregnancy test results).*
6. *History of uncontrolled asthma, allergy to vaccines or vaccine ingredients, and severe adverse reactions to vaccines, such as urticaria, dyspnea, and angioneurotic edema.*
7. *History of blood disorders contraindicating intramuscular injection.*
8. *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.*
9. *History of confirmed or suspected immunosuppressive or immunodeficient state or in the previous 4 weeks received a treatment likely to alter the immune response (intravenous immunoglobulins, blood-derived products, or long-term corticosteroid therapy (> 2 weeks)).*
10. *History of uncontrolled epilepsy or other progressive neurological disorders, such as Guillain-Barre Syndrome.*
11. *Subjects receive any vaccination (other than COVID-19 vaccine) within 1 month before and after IP immunization.*

12. *Subjects plan to move from the study area before the end of study period.*

11. ***Endpoint* Uji Klinik** : *Primary Endpoints*:

- *Geometric Mean Titer (GMT) and GMT ratio of neutralizing antibody to the SARS-CoV-2 measured by wild-type virus neutralization assay (against delta variant) at 14 days after two-dose primary series.*
- *Seroconversion rate of neutralizing antibody to the SARS-CoV-2 measured by wild-type virus neutralization assay (against delta variant) at 14 days after two-dose primary series.*
- *Seropositive rate of neutralizing antibody to the SARS-CoV-2 measured by wild-type virus neutralization assay (against delta variant) at 14 days after two-dose primary series.*
- *Comparison of GMT, seroconversion rate, seropositive rate of neutralizing antibody at 14 days after two-dose primary series between vaccine and control group.*

Secondary endpoints

Immunogenicity

- *GMT and seropositive rate of neutralizing antibody at 28 days, 3, 6, and 12 months after two-dose primary series.*
- *Seroconversion rate of neutralizing antibody at 28 days after two-dose primary series.*
- *GMT and seropositive rate of SARS-CoV-2 (RBD)-binding IgG antibody measured by Enzyme-Linked Immunosorbent Assay (ELISA) at 14, 28 days, 3, 6, and 12 months after two dose primary series.*
- *Seroconversion rate of neutralizing antibody at 14 days after two-dose primary series. Seroconversion rate of SARS-CoV-2 (RBD) binding IgG antibody at 14 and 28 days after two-dose primary series.*
- *Comparison of GMT, seroconversion rate, seropositive rate of neutralizing antibody & SARS-CoV-2 (RBD)-binding IgG antibody (ELISA) between vaccine and control group.*
- *Comparison of GMT, seroconversion rate, seropositive rate of neutralizing antibody & SARS-CoV-2 (RBD)-binding IgG antibody (ELISA) between three lot number of vaccine.*

Exploratory Study (Cellular immunity)

- *Positive rate of specific T-cell response (CD4, CD8, IFN-γ, TNF-α, IL-2, IL-4) at 14 days, 6 months and 12 months after two-dose primary series.*
- *GMT and seropositive rate of SARS-CoV-2 (RBD)-binding IgG antibody at 14 days, 6 months and 12 months after two-dose primary series.*
- *GMT and seropositive rate of neutralizing antibody at 14 days, 6 months and 12 months after two-dose primary series.*
- *Seroconversion rate of SARS-CoV-2 (RBD) binding IgG antibody at 14 days after two-dose primary series.*
- *Seroconversion rate of neutralizing antibody at 14 days after two-dose primary series.*

Safety

- *Number and percentage of subjects with solicited and unsolicited adverse events within 30 minutes, 7 days, and 28 days after each dose of primary series.*

- *Number and percentage of subjects with serious adverse events within 28 days after each dose of primary series.*
- *Number and percentage of subjects with serious adverse events until 12 months after two-dose primary series.*
- *Comparison the safety between vaccine and control group.*
- *Comparison the safety between three lot number of vaccine.*

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi terhadap protokol yang diajukan yang didukung oleh tim ahli melalui rapat pada tanggal 27 Mei 2022 dengan hasil sebagai berikut:

1. Berdasarkan data interim uji klinik fase I dan fase II, secara umum vaksin aman, kejadian tidak diinginkan (KTD) yang terjadi dapat ditoleransi dengan baik. Setelah suntikan kedua, vaksin dapat menginduksi respon imun yang lebih baik jika dibandingkan dengan vaksin pembanding.
2. Desain uji klinik menggunakan pembanding vaksin COVID-19 dengan platform sejenis untuk mengkonfirmasi imunogenisitas dan keamanan vaksin, dapat diterima.
3. Vaksin uji telah memenuhi persyaratan mutu.

Keputusan

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik No. RG.01.06.1.1.06.22.147 tanggal 6 Juni 2022