RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK FASE II/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 II/III yang diajukan telah didukung oleh studi non klinik berupa studi toksisititas akut dan subkronik pada tikus dan kelinci dan studi imunogenisitas pada mencit dan Macaca serta data keamanan dan imunogenisitas uji klinik fase 1.

Informasi Uji Klinik

1.	**Judul Protokol**	**:**	***A Phase 2/3, Double-Blind, Randomized, Placebo-Controlled Study of the Efficacy, Safety and Immunogenicity of SARS-CoV-2 Protein Subunit Recombinant Vaccine (Bio Farma) Adjuvanted with Alum+CpG 1018 in Healthy Populations Aged 18 Years and Above in Indonesia*** Versi 2.0 tanggal 14 Maret 2022
2.	**Produk Uji**	**:**	Vaksin SARS-COV-2 0,5 mL (12,5 mg dan 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**	**:**	Placebo, diberikan 2 kali secara intramuscular Produsen: PT. Bio Farma
4.	**Center / Peneliti**	**:**	1. Fakultas Kedokteran Universitas Andalas, Padang / dr. Asrawati, M.Biomed, SpA(K) 2. Fakultas Kedokteran Universitas Diponegoro, Semarang / dr. Yetty Movieta Nency, Sp.A.(K) 3. Fakultas Kedokteran Universitas Hasanuddin/ Dr.dr. Martira Maddeppungeng,Sp.A (K)
5.	**Sponsor**	**:**	PT. Bio Farma
6.	**Persetujuan Etik**	**:**	1. No. 669/UN.16.2/KEP-FK/2022 tanggal 28 Maret 2022 dari Komisi Etik Penelitian Fakultas Kedokteran Universitas Andalas. 2. No. 80/EC/KEPK/FK/UNDIP/IV/2022 tanggal 1 April 2022 dari Komisi Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Diponegoro. 3. No. 149/UN4.6.4.5.31/PP36/2022 tanggal 4 April 2022 dari Komite Etik Penelitian Universitas Hasanuddin
7.	**Desain Uji Klinik**	**:**	*Observer-blind, randomized, placebo-controlled prospective intervention study*
8.	**Jumlah Subjek**	**:**	*3,960 subjects for phase 2/3*

9. Tujuan Uji Klinik : *Primary Objective*

Phase 2 : To evaluate immunogenicity of the vaccine.
Phase 3 : To evaluate efficacy of the vaccine in preventing COVID-19 cases.

Secondary Objective
Phase 2
- *To evaluate safety of the vaccine.*
- *To compare safety and immunogenicity between vaccine and control group, to select the best formula candidate for phase*
- *To compare safety and immunogenicity between SARS-CoV-2 protein subunit recombinant vaccine and control group.*

Phase 3
- *To evaluate efficacy of the vaccine in preventing severe, critical and death COVID-19 cases.*
- *To evaluate safety of the vaccine.*
- *To evaluate lot-to-lot consistency using three batches of the vaccine by assessment of serum immune response.*
- *To evaluate antibody persistence at 3 and 6 months after primary series (for lot-to-lot consistency 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 selfreport 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:

Phase 2

- *Seropositive rate, seroconversion rate, GMT of anti-RBD antibody IgG titer (ELISA) at 14 days after two-dose primary series.*
- *Seropositive rate, seroconversion rate, GMT of neutralizing antibody at 14 days after two-dose primary series.*

Phase 3

Incidence of laboratory-confirmed COVID-19 cases by RT-PCR within 14 days to 6 months after two dose primary series.

Secondary endpoints

Phase 2

Safety

- *Number and percentage of subjects with solicited and unsolicited adverse events within 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.*
- *Comparison of number and percentage of subjects with adverse events between vaccine and control group within 28 days after each dose of primary series.*

For selected vaccine and placebo group included in phase 3:

- *Number and percentage of subjects with serious adverse events until 6 months after two-dose primary series.*

- *Immunogenicity*
- *Seropositive rate, seroconversion rate, GMT of anti-RBD antibody IgG titer (ELISA) at 28 days after two-dose primary series.*
- *Seropositive rate, seroconversion rate, GMT of neutralizing antibody at 28 days after two-dose primary series.*

- *Comparison of seropositive rate, seroconversion rate, GMT of anti-RBD antibody IgG titer (ELISA) at 14 and 28 days after two dose primary series between vaccine and control group.*
- *Comparison of seropositive rate, seroconversion rate, GMT of neutralizing antibody at 14 and 28 days after two-dose primary series between vaccine and control group.*

For selected vaccine and placebo group included in phase 3:

- *Seropositive rate, GMT of anti-RBD antibody IgG titer (ELISA) at 3 and 6 months after two dose primary series.*
- *Seropositive rate, GMT of neutralizing antibody at 3 and 6 months after two-dose primary series.*

Phase 3

Efficacy

- *Incidence of laboratory-confirmed COVID-19 cases (severe, critical, death) by RT-PCR within 14 days to 6 months after two-dose primary series.*
- *Exploratory: Genotyping of SARS-CoV-2 viral isolates from minimum 20% of laboratory confirmed COVID-19 cases by RT-PCR.*

Immunogenicity (lot-to-lot consistency subset)

- *Seropositive rate, GMT of anti-RBD antibody IgG titer (ELISA) at 28 days, 3 and 6 months after two-dose primary series.*
- *Seroconversion rate of anti-RBD antibody IgG titer (ELISA) at 28 days after two-dose primary series.Seropositive rate, GMT of neutralizing antibody at 28 days, 3 and 6 months after two-dose primary series.*
- *Seroconversion rate of neutralizing antibody at 28 days after two-dose primary series.*

Safety

- *Number and percentage of subjects with solicited and unsolicited adverse events within 28 days after each dose of primary series.*
- *Number and percentage of subjects with serious adverse events until 6 months after two-dose primary series.*
- *Comparison of number and percentage of subjects with adverse events between vaccine and control group within 28 days after each dose of primary series.*

Comparison of number and percentage of subjects with serious adverse events between vaccine and control group until 6 months after primary series.

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi terhadap protokol yang diajukan yang didukung oleh tim ahli melalui rapat pada tanggal 8 Maret 2022 dengan hasil sebagai berikut:

1. Berdasarkan data interim uji klinik fase I, secara umum kejadian tidak diinginkan (KTD) dapat ditoleransi dengan baik. Tidak terdapat kejadian tidak diinginkan serius (KTDS) pada semua subjek. Rerata hasil pemeriksaan laboratorium 7 hari setelah suntikan pertama masih dalam rentang normal. Perubahan nilai laboratorium pada beberapa subjek masih dapat diterima dan tidak signifikan secara klinis.
2. Protokol uji klinik fase II/III telah memenuhi persyaratan.
3. Vaksin uji telah memenuhi persyaratan mutu.

Keputusan

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik No. RG.01.06.1.3.04.22.62 tanggal 11 April 2022