RINGKASAN HASIL EVALUASI PERMOHONAN
PERSETUJUAN PELAKSANAAN UJI KLINIK FASE I
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 untuk meningkatkan imunogenisitas. Ajuvan CpG merupakan ajuvan baru produksi Dynavax USA.
2. Uji klinik fase 1 yang diajukan telah didukung oleh studi non klinik berupa studi toksisitas akut dan subkronik pada tikus dan kelinci serta studi imunogenisitas pada 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 (Adjuvanted with Alum+CpG 1018) in Healthy Populations Aged 18 Years and Above in Indonesia*** Versi 2.0 tanggal 9 Februari 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 dan 1500 mcg CpG 1018) diberikan 2 kali secara intramuskular Produsen: PT. Bio Farma
3.	**Produk Pembanding**	:	Vaksin SARS-CoV-2 inactivated 600 SU (Coronavac) diberikan 2 kali secara intramuskular Produsen: Sinovac
4.	**Center / Peneliti**	:	1. Departemen Ilmu Kesehatan Anak, Fakultas Kedokteran Universitas Indonesia / Prof. Dr.dr. Rini Sekartini, SpA (K) 2. Fakultas Kedokteran Universitas Diponegoro, Semarang / dr. Yetty Movieta Nency, Sp.A.(K)
5.	**Sponsor**	:	PT. Bio Farma
6.	**Persetujuan Etik**	:	1. No. 121/UN2.F1/ETIK/PPM.00.02/2022 Tanggal 7 Februari 2022 dari Komite Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Indonesia – RSUPN Dr. Cipto Mangunkusumo untuk protokol versi 1.b tanggal 6 Februari 2022. 2. No. 24/EC/KEPK/FK-UNDIP/I/2022 Tanggal 28 Januari 2022 dari Komite Etik Penelitian Kesehatan Universitas Diponegoro Fakultas Kedokteran untuk protokol versi 1a tanggal 26 Januari 2022.
7.	**Desain Uji Klinik**	:	*Observer-blind, randomized, controlled prospective intervention study*
8.	**Jumlah Subjek**	:	*175 subjects will be recruited in this study: 125 subjects in main study subset and 50 subjects in cellular immunity subset.*
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.*

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- *To evaluate serious adverse events until 6 months after last dose.*
- *To evaluate preliminary immunogenicity of the SARS-CoV-2 protein subunit recombinant vaccine.*
- *To compare safety and immunogenicity between SARS-CoV-2 protein subunit recombinant vaccine and control group.*

Kriteria Eligibilitas : **Kriteria Inklusi / *Inclusion criteria***

1. *Clinically healthy subjects aged 18 – 70 years.*
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 RT PCR test for SARS-CoV-2 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 immuneresponse (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.*

***Endpoint* uji klinik** : *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.*
- *Number and percentage of subjects with serious adverse events until 6 months after last dose.*
- *Comparison of number and percentage of subjects with adverse events between vaccine and control group within 28 days after each dose.*
- *Comparison of number and percentage of subjects with serious adverse events between vaccine and control group until 6 months after last dose.*
- *Any deviation from routine laboratory evaluation that probably related to the dosing 7 days after the first dose and 14 days after the second dose (in main study subset).*
- *The change of IL-6 in serum 7 days after the first dose and 14 days after the second dose (in main study subset).*

Immunogenicity
- *Seropositive rate and GMT anti-RBD antibody IgG titer (ELISA) at baseline, 14 days and 28 days after the second dose.*
- *Seroconversion of anti-RBD antibody IgG titer (ELISA) at 14 days and 28 days after the second dose.*
- *Seropositive rate and GMT of neutralizing antibody titer at baseline, 14 days and 28 days after the second dose.*
- *Seroconversion of neutralizing antibody titer at day at 14 days and 28 days after the second dose.*
- *Comparison of immunogenicity between vaccine and control group at 14 days and 28 days after the second dose.*

Cellular immunity
Positive rate of specific T-cell response (CD4, CD8, IFN-γ, TNF-α, IL-2, IL-4) 14 days after second dose

Ringkasan Hasil Evaluasi
Badan POM telah melakukan evaluasi terhadap protokol yang diajukan yang didukung oleh tim ahli melalui rapat pada tanggal 9 Februari 2022 dengan hasil sebagai berikut

1. Berdasarkan hasil uji non klinik pada mencit, tikus dan macaca, vaksin dapat ditoleransi dengan baik dan menghasilkan respon imun antibodi yang lebih baik dari pembandingnya. Hasil uji tantang juga menunjukkan bahwa vaksin dapat memberikan proteksi yang lebih baik daripada plasebo dan Vaksin Coronavac.
2. Desain uji klinik fase 1 untuk mengevaluasi keamanan 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. B-RG.01.06.1.1.02.22.22 tanggal 14 Februari 2022

Dirilis oleh BPOM 14 Februari 2022