RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN SARS-COV-2 AJUVAN ALUM + CYTOSINE-PHOSPHATE-GUANINE (CPG)
PRODUKSI PT. BIO FARMA
SEBAGAI VAKSIN BOOSTER PADA DEWASA

Informasi Umum

1. Vaksin SARS-CoV-2 adalah vaksin dengan *platform* subunit protein yang dikembangkan oleh PT. Bio Farma menggunakan seed rekombinan protein dari *Baylor College of Medicine (BCM)* menggunakan ajuvan alum+CpG.
2. Uji klinik vaksin sebagai booster pada dewasa telah didukung data khasiat keamanan pada pemberian primer melalui uji klinik fase I, II dan III.

Informasi Uji Klinik

1.	**Judul Protokol**	:	***Observer-Blind, Randomized, Controlled Study of Immunogenicity & Safety of SARS-Cov-2 Protein Subunit Recombinant Vaccine (Bio Farma) as a Booster Dose Against COVID-19 in Adults 18 Years of Age and Older*** Versi 1.a dated 25 July 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 1 kali secara intramuskular Produsen: PT. Bio Farma
3.	**Produk Pembanding**	:	Pfizer-BioNTech Covid-19 Vaccine (30 mcg vaksin COVID-19 mRNA dalam 0,3 ml), diberikan 1 kali secara intramuscular Produsen: Serum Institute of India
4.	**Center / Peneliti**	:	1. Departemen Ilmu Kesehatan Anak, Fakultas Kedokteran Universitas Padjadjaran / Prof. Dr. Kusnandi Rusmil, dr., SpA(K), MM 2. Departemen Ilmu Kesehatan Anak, Fakultas Kedokteran Universitas Udayana / Dr. dr. I Gusti Ayu Trisna Windiani, SpA(K)
5.	**Sponsor**	:	PT. Bio Farma
6.	**Persetujuan Etik**	:	1. No. LB.02.01/X.6.5/256/2022 tanggal 12 Agustus 2022 dari Komite Etik Penelitian RSUP Dr. Hasan Sadikin Bandung. 2. No. 2161/UN14.2.2.VII.14/LT/2022 tanggal 8 Agustus 2022 dari Komisi Etik Penelitian Fakultas Kedokteran Universitas Udayana.
7.	**Desain Uji Klinik**	:	*Observer-blind, randomized, active-controlled prospective intervention study*
8.	**Jumlah Subjek**	:	*900 subjects who had received complete primary doses of authorized/approved inactivated (Sinovac®), mRNA (Pfizer®), or viral vector COVID-19 vaccine (AstraZeneca®)*
9.	**Tujuan Uji Klinik**	:	*Primary Objective* *To evaluate immunogenic non-inferiority immune response of SARS-CoV-2 neutralizing antibody of Bio Farma vaccine compared to vaccine control at 14 days after booster dose.* *Secondary Objective* - *To evaluate SARS-CoV-2 (RBD)-binding IgG antibody titer before and 14 days after booster dose of Bio Farma vaccine.* - *To evaluate antibody persistence at 6 months after booster dose of Bio Farma vaccine.* - *To evaluate safety profile after booster dose of Bio Farma vaccine.*

- *To compare safety and immunogenicity between Bio Farma vaccine and control group.*

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

1. *Clinically healthy subjects aged 18 years and above.*
2. *Subjects who have previously received complete primary series of authorized/approved inactivated (Sinovac®), mRNA (Pfizer®), or viral vector COVID-19 vaccine (AstraZeneca®) with the last dose administered a minimum of 6 months prior to inclusion but not longer than 10 months prior to inclusion.*
3. *Subjects have been informed properly regarding the study and signed the informed consent form.*
4. *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. *Subject who has received booster dose of COVID-19 vaccine.*
3. *Subject who has history of COVID-19 in the last 3 months (based on anamnesis or other examinations). Evolving mild, moderate, or severe illness, especially infectious disease, or fever (body temperature ≥37.5℃, measured with infrared thermometer/thermal gun).*
4. *Women who are pregnant or planning to become pregnant during the study period (judged by self report of subjects and urine pregnancy test results).*
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 asthma, history of allergy to vaccines or vaccine ingredients, and severe adverse reactions to vaccines, such as urticaria, dyspnea, and angioneurotic edema.*
7. *History of uncontrolled coagulopathy or 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. *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)).*
10. *Subjects who have 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 omicron variant) at 14 days after booster vaccination.

Secondary endpoints
Immunogenicity
- *Seropositive rate of neutralizing antibody at baseline (before booster dose), 14 days and 6 months after booster vaccination.*
- *Seroconversion rate of neutralizing antibody at baseline (before booster dose) and 14 days after booster vaccination.*
- *Seropositive rate and Geometric means of titers (GMTs) of SARS-CoV-2 (RBD)-binding IgG antibody measured by Enzyme-Linked Immunosorbent Assay (ELISA) at baseline (before booster dose), 14 days and 6 months after booster vaccination.*
- *Seroconversion rate of SARS-CoV-2 (RBD)-binding IgG antibody measured by Enzyme-Linked Immunosorbent Assay (ELISA) at baseline (before booster dose) and 14 days after booster vaccination*
- *Comparison of GMTs, seroconversion rate, seropositive rate of SARS-CoV-2 (RBD)-binding IgG antibody and neutralizing antibody between vaccine and control group.*

Safety
- *Local reaction and systemic events occurring within 30 minutes after booster vaccination.*
- *Local reaction and systemic events occurring within 7 days after booster vaccination.*
- *Local reaction and systemic events occurring within 28 days after booster vaccination.*
- *Any serious adverse event occurring from inclusion until 6 months after booster vaccination.*
- *Comparison the safety between vaccine and control group*

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi terhadap pengajuan protokol uji klinik yang didukung oleh tim ahli melalui rapat pada tanggal gal 8 Juli 2022 dengan hasil sebagai berikut:

1. Berdasarkan data interim uji klinik fase III secara umum vaksin SARS-CoV-2 produksi PT Biofarma aman dan dapat menginduksi respon imun yang non inferior dibandingkan Vaksin Pembanding Covovax pada 14 hari setelah suntikan kedua.
2. Desain uji klinik vaksin *booster* heterolog dapat diterima.
3. Vaksin memenuhi persyaratan mutu.

Keputusan
Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik No. RG.01.06.1.1.08.22.206 tanggal 30 Agustus 2022