RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN INDOVAC PRODUKSI PT BIO FARMA
SEBAGAI VAKSIN BOOSTER HOMOLOG PADA DEWASA

Informasi Umum

1. IndoVac adalah vaksin SARS-CoV-2 dengan platform subunit protein yang dikembangkan oleh PT. Bio Farma bekerja sama dengan Baylor College of Medicine (BCM). Vaksin uji menggunakan *adjuvant* Alum dan *Cytosine-Phosphate-Guanine oligodeoxynucleotides* (CpG)-1018.
2. Vaksin IndoVac telah mendapatkan *Emergency Use Authorization* (EUA) tanggal 24 September 2022 sebagai vaksin primer dewasa dan Surat Persetujuan Perubahan (SPP) tanggal 3 November 2022 sebagai booster dewasa pada primer Sinovac, 18 Februari 2023 pada primer AstraZeneca, dan 21 April 2023 pada primer Pfizer.
3. PT. Bio Farma selaku Sponsor mengajukan persetujuan pelaksanaan uji klinik untuk mengevaluasi respon imun dan keamanan pemberian vaksin booster IndoVac pada subjek dewasa usia 18 tahun ke atas yang telah mendapatkan vaksin IndoVac primer lengkap dalam 12-18 bulan sebelumnya. Subjek yang akan direkrut merupakan subjek yang mengikuti uji klinik fase III IndoVac primer.

Informasi Uji Klinik

1.	Judul Protokol	:	***Immunogenicity & Safety of IndoVac® as a Homologous Booster Dose Against COVID-19 in Adults Aged 18 Years and Above in Indonesia*** *Protokol Number* CoV2-Booster 0323, *Version* 1.a, *Dated* 26 June 2023
2.	Produk Uji	:	IndoVac ® 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	:	-
4.	*Center* / Peneliti	:	Fakultas Kedokteran Universitas Diponegoro / dr. Yetty Movieta Nency, Sp.A(K) *Recruitment site:* Puskesmas Pringapus, Ungaran dan Puskesmas Maranggen I, Demak
5.	Sponsor / ORK	:	PT. Bio Farma / PT. Equilab International
6.	Persetujuan Etik	:	No. 14/KEPK/FK-UNDIP/VII/2023 tanggal 26 Juni 2023 dari Komisi Etik Penelitian Kesehatan FK Universitas Diponegoro
7.	Desain Uji Klinik	:	*Open-label/unblinded clinical trial, prospective interventional study, single arm, pre-post study.*
8.	Jumlah Subjek	:	*150 subjects aged 18 years and above will be recruited in this clinical trial. Immunogenicity (neutralization antibodies and SARS-CoV-2 RBD IgG) and safety observations were carried out up to 12 months after the booster.*
9.	Tujuan Uji Klinik	:	***Primary Objective*** *To evaluate immunogenicity of IndoVac® by neutralizing antibody before and at 14 days after booster dose*

Secondary Objectives

1. *To evaluate immunogenicity of IndoVac® by neutralizing antibody at 28 days after booster dose*
2. *To evaluate immunogenicity of IndoVac® by RBD- binding IgG antibody before, at 14 days and 28 days after booster dose*
3. *To evaluate antibody persistence of IndoVac® at 3, 6, and 12 months after booster dose*
4. *To evaluate safety of IndoVac® after booster dose*

10. Kriteria Eligibilitas : ***Inclusion Criteria***

1. *Clinically healthy subjects aged 18 years and above.*
2. *Subjects had previously received complete primary doses of IndoVac® with the last dose administered minimum 12 months but no longer than 18 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.*

Exclusion Criteria

1. *Subjects concomitantly enrolled or scheduled to be enrolled in another trial.*
2. *Subjects had received booster dose of COVID-19 vaccine.*
3. *History of COVID-19 within 3 months prior to enrollment (based on anamnesis or other examinations).*
4. *Evolving mild, moderate, or severe illness, especially infectious disease, or fever (body temperature ≥37.5°C, 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 uncontrolled coagulopathy or blood disorders contraindicating intramuscular injection.*
8. *Patients with serious chronic diseases (serious cardiovascular diseases, uncontrolled hypertension or diabetes, liver or 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 had 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 had received any vaccination (other than COVID-19 vaccine) within 1 month before IP immunization.*
12. *Subjects plan to move from the study area before the end of study period.*

11. *Endpoint* Uji Klinik : ***Primary Evaluation Criteria***

1. *Geometric Mean Titer (GMT) and seropositive rate of SARS-CoV-2 neutralizing antibody against Omicron variant at baseline (before booster dose) and 14 days after booster dose.*
2. *Geometric Mean Fold Ratio (GMFR) and seroconversion rate of SARS-CoV-2 neutralizing antibody against Omicron variant at 14 days after booster dose.*

Secondary Evaluation Criteria

Immunogenicity

1. *Geometric Mean Titer (GMT) and seropositive rate of SARS-CoV-2 neutralizing antibody against Omicron variant at 28 days, 3 months, 6 months, and 12 months after booster dose.*
2. *Geometric Mean Fold Ratio (GMFR) and seroconversion rate of SARS-CoV-2 neutralizing antibody against Omicron variant at 28 days after booster dose.*
3. *Geometric Mean Titer (GMT) and seropositive rate of SARS-CoV-2 RBD-binding IgG antibody at baseline, 14 days, 28 days, 3 months, 6 months, and 12 months after booster dose.*
4. *Geometric Mean Fold Ratio (GMFR) and seroconversion rate of SARS-CoV-2 RBD-binding IgG antibody at 14 days and 28 days after booster dose.*

Safety

1. *Number and percentage of subjects with solicited and unsolicited Adverse Events (AEs) within 30 minutes, 7 days, until 28 days after booster dose.*
2. *Number and percentage of subjects with Serious Adverse Events (SAEs) until 12 months after booster dose.*
3. *Number and percentage of subjects with Adverse Events of Special Interest (AESIs) until 12 months after booster dose.*

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol uji klinik Vaksin IndoVac sebagai vaksin *booster* homolog pada dewasa untuk COVID-19, yang didukung oleh tim ahli melalui rapat pada tanggal 26 Mei 2023 dengan hasil sebagai berikut:

1. Laporan interim uji klinik vaksin primer IndoVac dengan pembanding aktif vaksin Covovax pada subjek berusia 18 tahun ke atas, menunjukkan bahwa vaksin IndoVac memiliki tolerabilitas dan imunogenisitas yang sebanding dengan Covovax.
2. Kejadian Tidak Diinginkan (KTD) yang paling sering muncul yaitu nyeri di lokasi penyuntikan dan nyeri otot dengan intensitas ringan. Tidak ditemukan efek samping produk uji yang serius, KTD yang menjadi perhatian khusus/ *Adverse Events Special Interest* (AESI), ataupun kejadian COVID-19 yang berat. Terdapat peningkatan respon imun baik humoral (antibodi netralisasi dan imunoglobulin-G) maupun seluler. Peningkatan ini sebanding pada kelompok IndoVac dan Covovax.

3. Desain uji klinik *pre-posttest* dengan interpretasi penerimaan yang jelas sebagaimana protokol dapat diterima, desain sejenis juga telah digunakan untuk pengembangan vaksin *booster* lain.
4. 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 Nomor RG.01.06.1.3.07.23.23 tanggal 18 Juli 2023.