RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN INDOVAC PRODUKSI PT BIO FARMA
SEBAGAI VAKSIN BOOSTER PADA ANAK USIA 12-17 TAHUN

Informasi Umum

1. IndoVac adalah vaksin SARS-CoV-2 dengan platform subunit protein yang dikembangkan oleh PT. Bio Farma menggunakan *seed* vaksin dari Baylor College of Medicine (BCM). Vaksin uji menggunakan *adjuvant* Alum dan *Cytosine-Phosphate-Guanine oligodeoxynucleotides* (CpG)-1018.
2. PT. Bio Farma selaku Sponsor mengajukan persetujuan pelaksanaan uji klinik (PPUK) fase II untuk mengevaluasi respon imun dan keamanan pemberian vaksin booster IndoVac pada subjek remaja usia 12-17 tahun yang telah mendapatkan vaksin Sinovac primer lengkap dalam 6-12 bulan sebelumnya. IndoVac telah memperoleh EUA sebagai vaksin primer dan booster heterolog (vaksin primer Sinovac) untuk dewasa usia 18 tahun ke atas. Uji klinik vaksin primer pada anak usia 12-17 tahun sedang berlangsung dan telah diperoleh laporan interim.
3. Pada saat pengajuan, belum terdapat vaksin COVID-19 yang mendapatkan EUA sebagai booster untuk anak usia 12-17 tahun. Vaksin COVID-19 yang sudah disetujui untuk booster homolog pada anak usia 16 tahun ke atas adalah Comirnaty.

Informasi Uji Klinik

1.	Judul Protokol	:	***Immunogenicity and Safety of IndoVac® as a Heterologous Booster Dose Against COVID-19 in Children 12-17 Years of Age*** No. protokol CoV2-Booster-Children-0222, Versi 1.a, Tanggal 31 Januari 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	:	Departemen Ilmu Kesehatan Anak Fakultas Kedokteran Universitas Padjadjaran/RSHS / Dr. Eddy Fadlyana, dr.,SpA(K), M Kes
5.	Sponsor / ORK	:	Bio Farma (Persero) / PT Equilab International
6.	Persetujuan Etik	:	No. LB.02.01/X.6.5/465/2022 Tanggal 2022-12-20 dari Komite Etik Pusat Penelitian Kesehatan, Fakultas Kedokteran Universitas Padjajaran – Rumah Sakit Hasan Sadikin
7.	Desain Uji Klinik	:	*Open label prospective intervention study.*
8.	Jumlah Subjek	:	*150 subjects who had received complete primary doses of inactivated (Sinovac®) COVID-19 Vaccine.*
9.	Tujuan Uji Klinik	:	***Primary Objectives*** *To evaluate immune response to SARS-CoV-2 neutralizing antibody of IndoVac® before and 14 days after booster dose.* ***Secondary Objectives*** - *To evaluate SARS-CoV-2 (RBD)-binding IgG antibody titer before and 14 days after booster dose of IndoVac®.* - *To evaluate antibody persistence at 3, 6, and 12 months after booster dose of IndoVac®* - *To evaluate safety profile after booster dose of IndoVac®*

10. Kriteria Eligibilitas :

Inclusion criteria

1. *Clinically healthy children 12-17 years of age.*
2. *Subjects who have previously received complete primary series of inactivated (Sinovac®) COVID-19 vaccine with the last dose administered a minimum of 6 months prior to inclusion but not longer than 12 months prior to inclusion.*
3. *Parent/legal guardian and subject has been informed properly regarding the study, and signed the informed consent form (parent/legal guardian) and assent form (subject).*
4. *Parent and/or legal guardian will commit to comply with the instructions of the investigator and the schedule of the trial.*

Exclusion criteria

1. *Subject 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).*
4. *Evolving mild, moderate or severe illness, especially infectious disease or fever (body temperature ≥37.5℃, measured with infrared thermometer/thermal gun).*
5. *History of uncontrolled asthma, history of allergy to vaccines or vaccine ingredients, and severe adverse reactions to vaccines, such as urticaria, dyspnea, and angioneurotic edema.*
6. *History of uncontrolled coagulopathy or blood disorders contraindicating intramuscular injection.*
7. *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.*
8. *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)).*
9. *Subjects who have history of uncontrolled epilepsy or other progressive neurological disorders, such as Guillain-Barre Syndrome.*
10. *Subjects receive any vaccination (other than COVID-19 vaccine) within 1 month before and after IP immunization.*
11. *Female who are pregnant or planning to become pregnant during the study period (judged by self-report of subjects and urine pregnancy test results).*
12. *Subjects plan to move from the study area before the end of study period.*

11. *Endpoint* Uji Klinik :

Primary Evaluation Criteria

Geometric Mean Titer (GMT) and GMFR of neutralizing antibody to the SARS-CoV-2, measured by virus neutralization assay (against omicron variant) at 14 days after booster vaccination.

Secondary Evaluation Criteria

Immunogenicity

1. *Seropositive rate of neutralizing antibody at baseline (before booster dose), 14 days, 3 months, 6 months, and 12 months after booster vaccination.*
2. *Seroconversion rate of neutralizing antibody at baseline (before booster dose) and 14 days after booster vaccination.*
3. *Seropositive rate, Geometric means of titers (GMTs) and GMFR of SARS-CoV-2 (RBD)-binding IgG antibody measured by chemiluminescent microparticle immunoassay (CMIA) at baseline (before booster dose), 14 days, 3 months, 6 months, and 12 months after booster vaccination.*
4. *Seroconversion rate of SARS-CoV-2 (RBD)-binding IgG antibody measured by chemiluminescent microparticle immunoassay (CMIA) at baseline (before booster dose) and 14 days after booster vaccination*
5. *Geometric Mean Titer (GMT) and GMFR of neutralizing antibody to the SARS-CoV-2, measured by virus neutralization assay (against omicron variant) at 3 months, 6 months, and 12 months after booster vaccination.*

Safety

1. *Local reaction and systemic events occurring within 30 minutes after booster vaccination.*
2. *Local reaction and systemic events occurring within 7 days after booster vaccination.*
3. *Local reaction and systemic events occurring within 14 days after booster vaccination.*
4. *Local reaction and systemic events occurring within 28 days after booster vaccination.*
5. *Any serious adverse event occurring from inclusion until 12 months after booster vaccination.*

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol uji klinik Vaksin IndoVac sebagai vaksin *booster* pada anak usia 12-17 tahun untuk COVID-19, yang didukung oleh tim ahli melalui rapat pada tanggal 20 Desember 2022, dengan hasil sebagai berikut:

1. Laporan interim uji klinik vaksin primer IndoVac dibandingkan dengan pembanding aktif Covovax pada remaja usia 12-17 tahun, tidak terdapat perbedaan yang signifikan antara insiden reaksi lokal dan sistemik pada kedua kelompok. Kejadian Tidak Diinginkan (KTD) yang paling sering berupa nyeri pada lokasi penyuntikan dan nyeri otot. Sebagian besar KTD yang dilaporkan bersifat ringan. Tidak terdapat Efek Samping Produk Uji yang Serius. Secara umum, profil keamanan IndoVac cukup baik untuk diberikan pada usia 12-17 tahun. Pemberian IndoVac menyebabkan peningkatan respon imun yang sebanding dengan pembanding aktifnya.

2. Desain uji klinik *pre-posttest* dapat diterima, desain ini juga telah digunakan untuk pengembangan vaksin COVID-19 *booster* lain. Penggunaan platform protein subunit sebagai booster heterologous terhadap vaksin primer *inactivated* memiliki *potential benefit* sebagaimana *Interim Recommendations for Heterologous COVID-19 Vaccine Schedule,* WHO tanggal 16 Desember 2021.
3. 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.01.06.1.3.02.23.09 tanggal 13 Februari 2023.