RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN MERAH PUTIH-UA SARS-COV-2 PRODUKSI PT. BIOTIS
SEBAGAI VAKSIN BOOSTER HETEROLOG PADA REMAJA

Informasi Umum

1. Vaksin Merah Putih – UA SARS-CoV-2 dengan nama dagang Vaksin Inavac dikembangkan oleh Universitas Airlangga (UNAIR) bekerja sama dengan PT. Biotis.
2. Vaksin Inavac telah disetujui sebagai vaksin primer dan *booster heterolog* (untuk vaksin primer Sinovac) pada dewasa melalui mekanisme *Emergency Use Authorization* (EUA). Saat ini sedang dilakukan uji klinik untuk indikasi remaja usia 12 – 17 tahun.

Informasi Uji Klinik

1.	**Judul Protokol**	:	***Immunobridging Study: Immunogenicity and Safety of Vaksin Merah Putih – UA SARS-CoV-2 (Vero Cell Inactivated) Vaccine as Heterologue Booster in Adolescent Subjects in Indonesia*** Versi 3b.0 tanggal 22 April 2023
2.	**Produk Uji**	:	Vaksin Merah Putih-UA SARS-COV-2 (SARS COV-2 Inactivated 5 mcg) diberikan 2 kali secara intramuskular Produsen: PT. Biotis
3.	**Produk Pembanding**	:	**-**
4.	**Center / Peneliti**	:	RSUD Dr. Soetomo, Surabaya / Dr. Dominicus Husada, dr., Sp.A(K)
5.	**Sponsor / ORK**	:	1. Badan Penelitian dan Pengembangan Kesehatan, Kementerian Kesehatan Republik Indonesia. 2. PT. Biotis 3. Universitas Airlangga (UNAIR)
6.	**Persetujuan Etik**	:	No. 0715/KEPK/VII/2023 tanggal 13 Juli 2023 dari Komite Etik Penelitian Kesehatan RSUD Dr. Soetomo Surabaya
7.	**Desain Uji Klinik**	:	*This is an open label trial. There will only be 1 group in the study. All subjects will receive INAVAC vaccine and be followed for 6 months*
8.	**Jumlah Subjek**	:	*250 subject adolescents age 12-17 years old, male and female.*
9.	**Tujuan Uji Klinik**	:	*Primary Objective* *To evaluate the humoral immunogenicity – neutralizing antibody profile after 28 days following vaccination with INAVAC vaccine as heterologue booster in healthy adolescents age 12-17 years old.* *Secondary Objective* - *To evaluate safety and reactogenicity at 7 and 28 days, 3 and 6 months following vaccination with INAVAC vaccine as heterologue booster in healthy adolescents age 12-17 years old.* - *To evaluate the humoral immune – neutralizing antibody response at 3 and 6 months following vaccination with INAVAC vaccine as heterologue booster in healthy adolescents age 12-17 years old.* - *To evaluate the humoral immune – IgG RBD SARS-CoV-2 antibody response at 28 days, 3 and 6 months following vaccination with INAVAC*

vaccine as heterologue booster in healthy adolescents age 12-17 years old.

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

1. *Healthy males and females, adolescents age 12-17 years old. Healthy status will be determined by the investigator based on medical history, clinical laboratory results, vital sign measurements, and physical examination at screening.*
2. *Subjects already received 2 (two) doses of CoronaVac inactivated vaccines at least 3 months prior to this study.*
3. *Subjects and the parents or guardian have been informed properly regarding the study and signed the informed consent form*
4. *Subject and the parents or guardian will commit to comply with the instructions of the investigator and the schedule of the trial*
5. *Participants agree not to donate bone marrow, blood, and blood products from the first study vaccine administration until 3 months after receiving the vaccine.*
6. *Participants and the parents or guardian must be willing to provide verifiable identification, has means to be contacted and to contact the investigator during the study.*

Kriteria Eksklusi / *Exclusion criteria*

1. *Subjects concomitantly enrolled or scheduled to be enrolled in another vaccine trial*
2. *Evolving mild, moderate, and severe illness, especially infectious diseases or fever (axillary temperature 37.5oC or more) concurrent or within 7 days prior to study vaccination. This includes respiratory or constitutional symptms consistent with SARS-CoV-2 (cough, sore throat, difficulty in breathing, etc)*
3. *Known history of allergy to any component of the vaccines*
4. *History of uncontrolled coagulopathy or blood disorders contraindicating intramuscular injection*
5. *Any autoimmune or immunodeficiency disease/condition*
6. *Subjects who have received in the previous 4 weeks a treatment likely to alter the immune response (intravenous immunoglobulin, blood derived products, long term corticosteroid – more than 2 weeks, and so on), OR anticipation of the need for immunosuppressive treatment within 6 months after last vaccination. The use of topical or nasal steroid will be permitted. Inhaled glucocorticoids are prohibited.*
7. *Unstable chronic disease, inclusive of uncontrolled hypertension, congestive heart failure, chronic obstructive pulmonary disease, asthma, chronic urticaria, diabetes requiring use of medicine. The final decision regarding this condition will be decided by the attending field clinicians or investigator.*
8. *Any abnormality or chronic disease which according to the investigator might interfere with the assessment of the trial objectives*

9. *Subjects already immunized with any other vaccines within 4 weeks prior and expect to receive other vaccines within 60 days following the first dose*
10. *Individuals who have a previously ascertained Covid-19 in the period of 1 month (for mild, moderate, or asymptomatic people) or 3 months (for severe Covid-19) before the first recruit of this study, or in a close contact in the last 14 days with confirmed case of Covid-19.*
11. *Positive test for SARS-CoV-2 (Antigen or PCR) at screening prior to the vaccination. Testing may be repeated during the screening period if exposure to positive confirmed case of SARS-CoV-2 is suspected, at the discretion of investigator.*
12. *History of alcohol or substance abuse*
13. *HIV patients.*
14. *Malignancy patients within 3 years prior to study vaccination.*
15. *Any neurological disease or history of significant neurological disorder such as meningitis, encephalitis, Guillain-Barre Syndrome, multiple sclerosis, etc*
16. *Vital sign abnormalities and clinical laboratory abnormalities as decided by the investigators. Vital sign measurements and clinical laboratory testing may be repeated before the final decision.*
17. *Women who are pregnant or who plan to become pregnant during the study.*
18. *Participant has major psychiatric problem or illness*
19. *Participant cannot communicate reliably with the investigator*
20. *Participant has contraindication to intramuscular injection and blood draws, such as bleeding disorders or phobia.*
21. *Participant had major surgery within 12 weeks before vaccination which will not be fully recovered, or has major surgery planned during the time participant is expected to participate in the study or within 6 months after the vaccination.*
22. *Any condition that in the opinion of the investigators would pose a helath risk to the subject if enrolled or could interfere with the evaluation of the vaccine or interpretation of the study results*
23. *Study team members.*
24. *Subject planning to move from the study area before the end of study period.*

11. Luaran Uji Klinik/*Endpoint* : **Luaran Primer /** *Primary Endpoints*:
Humoral Immune Reponse (Neutralizing antibody):
SARS-CoV-2 Neutralization: SARS-CoV-2 neutralizing titers in serum measured by a virus neutralization assay, at 28 days following vaccination with INAVAC vaccine as heterologue booster in healthy adolescents age 12-17 years old.

Luaran Sekunder / *Secondary endpoints*
Safety:

- *Solicited – clinical (local and systemic) adverse events for 7 and 28 days, 3 and 6 months following vaccination with INAVAC vaccine as heterologue booster in healthy adolescents age 12-17 years old.*
- *Unsolicited adverse events for 7 and 28 days, 3 and 6 months following vaccination with INAVAC vaccine as heterologue booster in healthy adolescents age 12-17 years old.*
- *Serious adverse event (SAE) throughout the study*

Humoral Immunogenicity:

- *SARS-CoV-2 Neutralization: SARS-CoV-2 neutralizing titers in serum measured by a virus neutralization assay for 3 and 6 months following vaccination with INAVAC vaccine as heterologue booster in healthy adolescents age 12-17 years old.*
- *IgG RBD SARS-CoV-2 (CLIA): analysis of IgG RBD SARS-CoV-2 antibodies for 28 days, 3 and 6 months following vaccination with INAVAC vaccine as heterologue booster in healthy adolescents age 12-17 years old.*

Exploratory Evaluation Criteria

Whole genome sequencing (WGS) of S protein of SARS-CoV-2 virus from all positive Covid-19 cases during the study

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi terhadap protokol yang diajukan yang didukung oleh tim ahli melalui rapat pada tanggal 16 Maret 2023 dengan hasil sebagai berikut:

1. Vaksin telah memiliki efikasi dan keamanan pada subjek dewasa dan disetujui sebagai vaksin primer dan booster heterolog (untuk primer Sinovac) pada dewasa.
2. Desain uji klinik untuk *booster* pada remaja dapat diterima.
3. Vaksin memenuhi persyaratan mutu.

Keputusan

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik (PPUK) No. RG.01.06.1.3.09.23.34 tanggal 13 September 2023