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

Informasi Umum

1. Vaksin Covid-19 UNAIR *Inactivated* atau Vaksin Merah Putih dikembangkan oleh Universitas Airlangga (UNAIR) bekerja sama dengan PT. Biotis Pharmaceuticals Indonesia.
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**	:	***Immunobridging Study: Immunogenicity and Safety of Vaksin Merah Putih – UA SARS-CoV-2 (Vero Cell Inactivated) Vaccine as Heterologue Booster in Adult Subjects in Indonesia*** Versi 1.c.0 tanggal 16 Agustus 2022
2.	**Produk Uji**	:	Vaksin Merah Putih-UA SARS-COV-2 (SARS COV-2 Inactivated 5 mcg), diberikan 1 kali secara intramuskular Produsen: PT. Biotis Pharmaceuticals Indonesia
3.	**Produk Pembanding**	:	Vaksin SARS-CoV-2 inactivated 600 SU (Coronavac), diberikan 1 kali secara intramuskular Produsen: Sinovac
4.	**Center / Peneliti**	:	RSUD Dr. Soetomo, Surabaya / Dr. dr. Dominicus Husada, DTM&H.,MCTM(TP).,SpA(K)
5.	**Sponsor / ORK**	:	1. Badan Penelitian dan Pengembangan Kesehatan, Kementerian Kesehatan Republik Indonesia. 2. PT. Biotis PT. Biotis Pharmaceuticals Indonesia 3. Universitas Airlangga (UNAIR)
6.	**Persetujuan Etik**	:	No. 0472/KEPK/VIII/2022 tanggal 19 Agustus 2022 dari Komite Etik Penelitian Kesehatan RSUD Dr. Soetomo Surabaya
7.	**Desain Uji Klinik**	:	*Observer blind randomized controlled trial*
8.	**Jumlah Subjek**	:	*350 subjects 18 years old and above*
9.	**Tujuan Uji Klinik**	:	*Primary Objective* *To evaluate the humoral immunogenicity profile – neutralizing antibody - after 28 days following vaccination with Vaksin Merah Putih – UA SARS-CoV-2 (Vero Cell Inactivated) vaccine as heterologue booster compared with CoronaVac administered intramuscularly in healthy adults age 18 year and above* *Secondary Objective* - *To evaluate safety and reactogenicity within 7 and 28 days, 3 and 6 months following vaccination with Vaksin Merah Putih – UA SARS-CoV-2 (Vero Cell Inactivated) vaccine as heterologue booster compared with CoronaVac administered intramuscularly in healthy adults age 18 year and above* - *To evaluate the humoral immune response – neutralizing antibody - at 3 and 6 months following vaccination with Vaksin Merah Putih – UA SARS-CoV-2 (Vero Cell Inactivated) vaccine as heterologue booster*

compared with CoronaVac administered intramuscularly in healthy adults age 18 year and above

- *To evaluate the humoral immune response – non neutralizing antibody - at 28 days, 3 and 6 months following vaccination with Vaksin Merah Putih – UA SARS CoV-2 (Vero Cell Inactivated) vaccine as heterologue booster compared with CoronaVac administered intramuscularly in healthy adults age 18 year and above*

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

1. *Healthy adults and elderly, males and females, 18 years of age and above. 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 6 months prior to this study.*
3. *Subjects have been informed properly regarding the study and signed the informed consent form*
4. *Subject will commit to comply with the instructions of the investigator and the schedule of the trial*
5. *Female subjects of childbearing potential must agree to consistently use any methods of contraception (except the periodic abstinence) from at least 21 days prior to enrollment and through 6 months after the vaccination.*
6. *Participants agree not to donate bone marrow, blood, and blood products from the vaccine administration until 3 months after receiving the vaccine.*
7. *Participants 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 symptoms 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. *Individuals who previously receive any booster vaccine against Covid-19.*
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 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 last dose of study vaccine administration.*
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. *Endpoint* Uji Klinik : *Primary Endpoints*:
Assessment of humoral immunogenicity (time frame: 28 days after the vaccination): SARS-CoV-2 neutralization antibody after vaccination with Vaksin Merah Putih – UA SARS-CoV-2 (Vero Cell Inactivated) vaccine as heterologue booster compared with CoronaVac administered intramuscularly in healthy adults age 18 year and above.

- *Percentage of subject's seroconversion (seronegative to seropositive OR with >4 times increasing antibody)*
- *Geometric mean titers (GMT) following two doses immunization (time frame 28 days after the second vaccination)*

Secondary endpoints
Safety:
- *Solicited and unsolicited - Clinical (Local reaction and systemic event) events after vaccination (time frame: 7 and 28 days, 3 and 6 months after the vaccination) with Vaksin Merah Putih – UA SARS-CoV-2 (Vero Cell Inactivated) vaccine as heterologue booster compared with CoronaVac administered intramuscularly in healthy adults age 18 year and above*
  - ☐ *Percentage of subjects with at least one of these adverse events, solicited and unsolicited, for 7 and 28 days, 3 and 6 months after the vaccination*
- *Any serious adverse events after vaccination (time frame: up to 6 months) with Vaksin Merah Putih – UA SARS-CoV-2 (Vero Cell Inactivated) vaccine as heterologue booster compared with CoronaVac administered intramuscularly in healthy adults age 18 year and above*
  - ☐ *Number and percentage of subjects with serious adverse events from inclusion until 6 months after the vaccination Immunogenicity*

Humoral Immunogenicity:
- *Assessment of humoral immunogenicity – neutralization antibody (time frame: 3 and 6 months) after the vaccination with Vaksin Merah Putih – UA SARS-CoV-2 (Vero Cell Inactivated) vaccine as heterologue booster compared with CoronaVac administered intramuscularly in healthy adults age 18 year and above*
  - ☐ *Percentage of subject's seroconversion (seronegative to seropositive OR with >4 times increasing antibody) (time frame 3 and 6 months after the vaccination)*
  - ☐ *Geometric mean titers (GMT) following the vaccination (time frame 3 and 6 months after the vaccination)*

Assessment of humoral immunogenicity – non neutralization antibody - SARS-CoV-2 binding antibody (CLIA) (time frame: 28 days, 3 and 6 months) after the vaccination with Vaksin Merah Putih – UA SARS-CoV-2 (Vero Cell Inactivated) vaccine as heterologue booster compared with CoronaVac administered intramuscularly in healthy adults age 18 year and above
  - ☐ *Percentage of subject's seroconversion (seronegative to seropositive OR with >4 times increasing antibody) (time frame 28 days, 3 and 6 months after the vaccination)*
  - ☐ *Geometric mean titers (GMT) following the vaccination (time frame 28 days, 3 and 6 months after the vaccination)*

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 12 Agustus 2022 dengan hasil sebagai berikut:

1. Berdasarkan data uji klinik fase I, II dan III, vaksin aman dan dapat menginduksi respon imun yang sebanding dengan vaksin pembanding.
2. Desain uji klinik untuk mengevaluasi imunogenisitas dan keamanan setelah pemberian booster dengan pembanding Coronavac dapat diterima.
3. Vaksin memenuhi persyaratan mutu.

Keputusan

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik No. RG.01.06.1.1.08.22.205 tanggal 26 Agustus 2022