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

**Informasi Umum**

1. Vaksin Inavac dikembangkan oleh Universitas Airlangga (UNAIR) bekerja sama dengan PT. Biotis. Pengembangan vaksin tersebut menggunakan virus SARS-CoV-2 yang diisolasi dari pasien COVID-19 di Surabaya.
2. Vaksin Inavac telah disetujui sebagai vaksin primer dan booster heterolog (untuk primer Sinovac) pada dewasa melalui mekanisme Emergency Use Authorization. Uji klinik yang diajukan untuk mengetahui Vaksin Inavac sebagai booster homolog dengan merekrut subjek yang telah mengikuti uji klinik Inavac sebagai vaksin primer.

**Informasi Uji Klinik**

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| 1. | Judul Protokol | : | ***Immunobridging Study: Immunogenicity and Safety of Inavac (Vaksin Merah Putih – UNAIR SARS-CoV-2 (Vero Cell Inactivated) Vaccine as Homologue Booster in Adult subjects Indonesia***<br>Versi 4a.0 tanggal 24 Agustus 2023 |
| 2. | Produk Uji | : | Vaksin Merah Putih-UA (Inavac), SARS COV-2 Inactivated 5 mcg, diberikan 2 kali secara intramuskular |
| 3. | Produk Pembanding | : | - |
| 4. | Center / Peneliti | : | RSUD Dr. Soetomo, Surabaya / Dr. Dominicus Husada, dr., Sp.A(K) |
| 5. | Sponsor / ORK | : | a. Badan Penelitian dan Pengembangan Kesehatan, Kementerian Kesehatan Republik Indonesia.<br>b. PT. Biotis<br>c. Universitas Airlangga (UNAIR) |
| 6. | Persetujuan Etik | : | No. 0817/KEPK/X/2023 tanggal 27 Oktober 2022 dari Komite Etik Penelitian Kesehatan RSUD Dr. Soetomo Surabaya |
| 7. | Desain Uji Klinik | : | *Open label trial. There will be only one group in the study* |
| 8. | Jumlah Subjek | : | *400 subjects 18 years old and above* |
| 9. | Tujuan Uji Klinik | : | *Primary Objective*<br>*To evaluate the humoral immunogenicity profile at 28 days following vaccination with INAVAC vaccine as homologue booster administered intramuscularly in healthy adults age 18 year and above*<br><br>*Secondary Objective*<br>- *To evaluate safety and reactogenicity at 7 and 28 days, 3 and 6 months following vaccination with INAVAC vaccine as homologue booster administered intramuscularly in healthy adults age 18 year and above* |

- *To evaluate the humoral immune response at 3 and 6 months following vaccination with INAVAC vaccine as homologue booster 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 Inavac vaccine (5 mcg), mostly during the phase I/II/III*
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 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. *Individuals who previously receive any booster vaccine against Covid-19 other than Inavac*
10. *Subjects already immunized with any other vaccines within 4 weeks prior and expect to receive other vaccines within 60 days following the first dose*
11. *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.*
12. *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.*
13. *History of alcohol or substance abuse*
14. *HIV patients.*
15. *Malignancy patients within 3 years prior to study vaccination.*
16. *Any neurological disease or history of significant neurological disorder such as meningitis, encephalitis, Guillain-Barre Syndrome, multiple sclerosis, etc*
17. *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.*
18. *Women who are pregnant or who plan to become pregnant during the study.*
19. *Participant has major psychiatric problem or illness*
20. *Participant cannot communicate reliably with the investigator*
21. *Participant has contraindication to intramuscular injection and blood draws, such as bleeding disorders or phobia.*
22. *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.*
23. *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*
24. *Study team members.*
25. *Subject planning to move from the study area before the end of study period.*

11. Luaran Uji Klinik*/Endpoint* : *Primary Endpoints*:

*Humoral Immune Reponse:*

- *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 homologue booster administered intramuscularly in healthy adults age 18 year and above*
- *IgG RBD SARS-CoV-2 antibodies measured by CLIA: analysis of antibodies binding to the SARS-CoV-2 S-protein, at 28 days following vaccination with INAVAC vaccine as homologue booster administered intramuscularly in healthy adults age 18 year and above*

*Secondary endpoints*
*Safety:*
- *Solicited – clinical (local and systemic) adverse events for 7 and 28 days, 3 and 6 month following vaccination with INAVAC vaccine as homologue booster administered intramuscularly in healthy adults age 18 year and above*
- *Unsolicited adverse events for 7 and 28 days, 3 and 6 months following vaccination with INAVAC vaccine as homologue booster administered intramuscularly in healthy adults age 18 year and above*
- *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 homologue booster administered intramuscularly in healthy adults age 18 year and above*
- *IgG RBD SARS-CoV-2 antibodies measured by CLIA: analysis of antibodies binding to the SARS-CoV-2 S-protein, for 3 and 6 months following vaccination with INAVAC vaccine as homologue booster administered intramuscularly in healthy adults age 18 year and above*

*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 17 September 2023 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 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.01.06.1.1.11.23.154 tanggal 20 November 2023