RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN SARS-COV-2 INACTIVATED FASE 3
PRODUKSI SINOVAC BIOTECH, CHINA

Informasi Umum

1. PT. Bio Farma mengajukan uji klinik fase III Vaksin SARS-CoV-2 bekerja sama dengan Sinovac Research & Development Co., Ltd., China. Uji klinik fase III Vaksin SARS-CoV-2 akan dilakukan di Indonesia dan beberapa negara yaitu Turki, Bangladesh, Chile dan Brazil (negara endemis) dengan protokol yang disesuaikan persyaratan dan kondisi masing-masing negara.
2. Pengajuan uji klinik Vaksin SARS-CoV-2 fase 3 didukung oleh uji nonklinik dan uji klinik fase1 dan 2.

Informasi Uji Klinik

1.	Judul Protokol	:	***A Phase III, Observer-blind, Randomized, Placebo-controlled Study of the Efficacy, Safety and Immunogenicity of SARS-CoV-2 Inactivated Vaccine in Healthy Adults Aged 18-59 Years in Indonesia*** (versi 2.0, 27 Juli 2020)
2.	Produk Uji	:	Vaksin SARS-CoV-2 Inactivated (SARS-CoV-2 antigen of 600 SU/0.5 mL) diberikan 2 kali secara intramuskular Produsen Sinovac Biotech, China
3.	Produk Pembanding	:	Vaksin Placebo diberikan 2 kali secara intramuskular Produsen Sinovac Biotech, China
4.	Center / Peneliti	:	Prof. Dr. Kusnandi Rusmil, dr., Sp.A(K)., MM / RSUP Dr. Hasan Sadikin/Fakultas Kedokteran Universitas Padjadjaran Bandung
5.	Sponsor / ORK	:	PT. Bio Farma
6.	Persetujuan Etik	:	No. 669/UN6.KEP/EC/2020 tanggal 27 Juli 2020 dari Komisi Etik Penelitian Universitas Padjadjaran, Bandung
7.	Desain Uji Klinik	:	*Observer-blind, randomized, placebo-controlled two arms parallel groups, prospective intervention study*
8.	Jumlah Subjek	:	*1620 subjects (18 – 59 years old)*
9.	Tujuan Uji Klinik	:	*Primary Objective* *To evaluate the efficacy of SARS-CoV-2 vaccine in preventing disease caused by SARS-CoV-2.* *Secondary Objective* - *To evaluate the efficacy of SARS-CoV-2 vaccine in preventing suspected cases.* - *To evaluate the safety of the SARS-CoV-2 vaccine.* - *To evaluate the immunogenicity of the SARS-CoV-2 vaccine* - *To evaluate lot-to-lot consistency using 3 batches of SARS-CoV-2 vaccine by assessment of serum immune response.*

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

1. *Clinically healthy adults aged 18 – 59 years.*
2. *Subjects have been informed properly regarding the study and signed the informed consent form.*
3. *Subjects will commit to comply with the instructions of the investigator and the schedule of the trial.*

Kriteria Eksklusi / *Exclusion criteria*

1. *Subjects concomitantly enrolled or scheduled to be enrolled in another trial.*
2. *Contact with novel coronavirus infected persons (positive for nucleic acid detection) within 14 days prior to the trial.*
3. *Contact to patients with fever or respiratory symptoms surrounding areas or from communities with reported cases within 14 days prior to the trial.*
4. *Two or more cases of fever and/or respiratory symptoms in a small area such as home, office, school and class within 14 days prior to the trial.*
5. *Evolving mild, moderate or severe illness, especially infectious disease or fever (body temperature ≥37.5℃, measured with infrared thermometer/thermal gun).*
6. *The result of RT-PCR of swab nasopharyngeal is positive*
7. *Reactive IgG and IgM for SARS-CoV-2 (by standardize rapid test).*
8. *Women who are lactating, pregnant or planning to become pregnant during the study period (judged by self-report of subjects and urine pregnancy test results).*
9. *History of asthma, history of allergy to vaccines or vaccine ingredients, and severe adverse reactions to vaccines, such as urticaria, dyspnea, and angioneurotic edema.*
10. *History of uncontrolled coagulopathy or blood disorders contraindicating intramuscular injection.*
11. *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.*
12. *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 immuneresponse (intravenous immunoglobulins, blood-derived products or long-term corticosteroid therapy (> 2 weeks)).*
13. *Subjects who have history of uncontrolled epilepsy or other progressive neurological disorders, such as Guillain-Barre Syndrome*
14. *Subjects receive any vaccination within 1 month before and after IP immunization.*

15. *Subjects plan to move from the study area before the end of study period.*

11. Luaran Uji Klinik/*Endpoint* : **Luaran Primer** */ Primary Endpoints*:
Incidence of laboratory-confirmed COVID-19 cases within 14 days to 6 months after the second dose.

Luaran Sekunder */ Secondary endpoints*

Efficacy
- *Incidence of suspected COVID-19 cases within 14 days to 6 months after the second dose.*
- *Incidence of laboratory-confirmed (severe cases,critical, death) within 14 days to 6 months after the second dose.*

Immunogenicity
- *Seroconversion rate and GMT anti-S antibody IgG titer (ELISA) on day 14 after two doses of vaccination*
- *Seroconversion rate and GMT anti-S antibody IgG titer (ELISA) on day 14 after two doses of vaccination between 3 batches of SARS-CoV-2 vaccine.*
- *Seropositive rate, GMT, seroconversion of neutralizing antibodies 14 days after two doses of vaccination.*
- *Seropositive rate, GMT, seroconversion of neutralizing antibodies 14 days after two doses of vaccination between 3 batches of SARS-CoV-2 vaccine.*

Exploratory Endpoints for Immunogenicity
- *Seroconversion rate, GMT of anti SARS-CoV-2 S antibody response (ELISA) 6 months after two doses of vaccination.*
- *Seropositive rate, GMT, and seroconversion of neutralizing antibodies 6 months* after after two doses of vaccination.

Safety
- Local *reaction and systemic events occurring within 30 minutes after each immunization.*
- *Local reaction and systemic events occurring within 14 days after each immunization.*
- *Local reaction and systemic events occurring after the 14 days to 28 days following the last vaccination will also be reported through.*
- *Any serious adverse event occurring from inclusion until 28 days after the last dose.*
- *Any serious adverse event occurring from inclusion until 6 months after the last dose*.

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol yang diajukan yang didukung oleh tim ahli melalui rapat pada tanggal 8 Juli 2020 dengan hasil sebagai berikut:

1. Berdasarkan uji nonklinik yang dilakukan berupa *single dose toxicity* (tikus), *active systemic anaphylaxis* (marmut), *repeated dose toxicity* (tikus dan macaca), *reproductive toxicity* (tikus)

dan imunogenisitas (mencit dan tikus) menunjukkan vaksin aman dan dapat ditoleransi dengan baik, serta dapat memberikan respon imun.

2. Uji klinik fase I dan II telah dilakukan di Cina dengan 2 schedule vaksinasi, yaitu pemberian hari ke-0 dan 14 dan pemberian hari ke-0 dan 28. Berdasarkan hasil pemberian hari ke-0 dan 14, menunjukkan vaksin memiliki keamanan yang dapat ditoleransi dan memberikan respon imun yang baik setelah dua kali suntikan.
3. Desain uji klinik yang diajukan dapat diterima. Uji klinik fase III di Indonesia akan dilakukan menggunakan schedule vaksinasi hari ke-0 dan 14, sesuai dengan hasil uji klinik fase I dan II yang telah diserahkan ke Badan POM.
4. Vaksin memenuhi persyaratan mutu.

Keputusan

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik (PPUK) No. RG.01.06.1.3.07.20.09 tanggal 27 Juli 2020.