RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
RECOMBINANT COVID-19 VACCINE (SF9 CELLS)
PRODUKSI WESTVAC BIOPHARM CO., LTD, CHINA

Informasi Umum

1. *Recombinant* COVID-19 *Vaccine* (Sf9 cells) merupakan vaksin protein rekombinan yang dikembangkan oleh West China Hospital of Sichuan University dan Chengdu WestVac Biopharm Co., Ltd, China. Vaksin ini menggunakan baculovirus sebagai vector dan mengekspresikan RBD spike protein SARS-CoV-2 pada sel Sf9. Vaksin ini telah terdaftar dalam *Draft Landscape of COVID-19 Candidate Vaccine*.
2. Uji klinik fase I telah dilaksanakan dan uji klinik fase II sedang dilakukan pada 900 subjek di China pada subjek dewasa dan subjek lansia serta telah diperoleh data interim keamanan dan imunogenisitas 30 hari.
3. Uji klinik fase III yang diajukan direncanakan dilakukan *multicenter* global di 6 negara yaitu Filipina, Pakistan, Kenya, Indonesia, Nepal dan Malaysia.

Informasi Uji Klinik

1.	Judul Protokol	:	***A global multicenter, randomized, double-blind, placebo-controlled, phase III clinical trial to evaluate the efficacy, safety, and immunogenicity of recombinant COVID-19 vaccine (Sf9 cells), for the prevention of COVID-19 in adults aged 18 years and older*** No. protokol JSVCT109, Versi 1.2, Tanggal 26 April 2021
2.	Produk Uji	:	Recombinant COVID-19 Vaccine (Sf9 cells) 40µg/1 mL/vial, diberikan 3 kali pada hari ke-0, 21, dan 42 secara intramuskular. Produsen: WestVac Biopharma Co., Ltd, Chengdu, China
3.	Produk Pembanding	:	Plasebo (AlOH) 0.42 mg/1 mL/vial, diberikan 3 kali pada hari ke-0, 21, dan 42 secara intramuskular Produsen: WestVac Biopharma Co., Ltd, Chengdu, China
4.	*Center* / Peneliti	:	1. RSUP Persahabatan/dr. Sita Andarini, Sp.P(K), Ph.D *Field site*: RS Permata Bekasi, RS TNI AU (RSAU) dr. Esnawan Antariksa, Jakarta Timur; RS Khusus Daerah Duren Sawit, Jakarta Timur; Puskesmas Ciketingudik, Bekasi; RS Pusat Pertamina (RSPP). 2. RS Universitas Airlangga/Prof. Dr. dr. Nasronudin, Sp.PD., K-PTI., FINASIM.
5.	Sponsor / ORK	:	WestVac Biopharma Co., Ltd dan West China Hospital of Sichuan University / PT. Equilab International
6.	Persetujuan Etik	:	1. No. 54.1.A/KEPK-RSUPP/06/2021 tanggal 9 Juni 2021 dari Komite Etik Penelitian Kesehatan Rumah Sakit Persahabatan 2. No. 15555/UN3.9.1/PT 2021 tanggal 21 Mei 2021 dari Komite Etik Penelitian Rumah Sakit Airlangga
7.	Desain Uji Klinik	:	*A randomized, double-blind, placebo-controlled, international multicenter clinical trial design will be adopted. This is a case-driven study. If 52 cases of COVID-19 (1/3), 104 cases of COVID-19(2/3) are observed during the study course, interim analysis will be made. A DSMB will be set up to monitor the safety data during the study.*
8.	Jumlah Subjek	:	*A total of 29,000 subjects aged 18 years and above, including 1,000 subjects in China (750 subjects aged 18-59 years and 250 subjects aged 60 years and above); and 28,000 subjects outside China (21,000 subjects aged 18-59 years and 7,000 subjects aged 60 years and above). Target recruitment in Indonesia will be 4000 subjects in total.*
9.	Tujuan Uji Klinik	:	***Primary Objectives*** ***Primary Efficacy Objective*** *Efficacy of recombinant COVID-19 vaccine (Sf9 cells) in preventing virologically confirmed (PCR positive) symptomatic COVID-19.*

Primary Safety Objective

1. *Safety of recombinant COVID-19 vaccine (Sf9 cells) in terms of SAE, MAAE and AESI in all participants from Day 0 through 6 months after completion of 3 doses vaccination.*
2. *Reactogenicity of recombinant COVID-19 vaccine (Sf9 cells) in all participants.*

Secondary Objectives

Secondary Efficacy Objectives

1. *Efficacy of recombinant COVID-19 vaccine (Sf9 cells) in preventing virologically confirmed (PCR positive) symptomatic COVID-19.*
2. *Efficacy of recombinant COVID-19 vaccine (Sf9 cells) in preventing severe COVID-19 or death caused by SARS-CoV-2 infection.*
3. *Efficacy of recombinant COVID-19 vaccine (Sf9 cells) in preventing virologically confirmed (PCR positive) hospitalized moderate, severe COVID-19 and death caused by SARS-CoV-2 infection.*
4. *Efficacy of recombinant COVID-19 vaccine (Sf9 cells) in preventing serologically confirmed SARS-CoV-2 infection or virologically confirmed (PCR positive) COVID-19 regardless of symptomatology or Severity.*

Secondary Safety Objective

Safety of recombinant COVID-19 vaccine (Sf9 cells) in terms of SAE, MAAE and AESI in all participants from Day 0 through 12 months after completion of 3 doses vaccination.

Secondary Immunogenicity Objective

Immunogenicity of recombinant COVID-19 vaccine (Sf9 cells) in the efficacy-extended safety-immunogenicity cohort.

Exploratory objectives

1. *Genotyping of SARS-CoV-2 virus nucleic acid sequence of COVID-19 cases.*
2. *Efficacy of recombinant COVID-19 vaccine (Sf9 cells) in preventing virologically confirmed (PCR positive) symptomatic COVID-19 in different age groups (18-59 group* and ≥60 group).

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

1. *Aged 18 years and older.*
2. *Able and willing (in the investigator's opinion) to comply with all study requirements.*
3. *Willing to allow the investigators to discuss the volunteer's medical history with their general practitioner/personal doctor and access all medical records which are relevant to study procedures.*
4. *Healthy adults, or stable-healthy adults who may have a pre-existing medical condition that does not meet any exclusion criteria. A stable medical condition is defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 3 months before enrollment.*
5. *For females of childbearing potential only, willingness to practice continuous effective contraception (see glossary) for 90 days after completion of 3 doses vaccination during the study, and have a negative pregnancy tests before each dose vaccination.*
6. *Note: nonchildbearing potential is defined as surgically sterile (history of bilateral tubal ligation, bilateral oophorectomy, hysterectomy) or postmenopausal (defined as amenorrhea for ≥ 12 consecutive months prior to Screening without an alternative medical cause). A follicle-stimulating hormone (FSH) level may be measured at the discretion of th investigator to confirm*

postmenopausal status.

7. *Males participating in this study who are involved in heterosexual sexual activity must agree to practice adequate contraception (see glossary) and refrain from donating sperm for 90 days after receiving the study vaccination.*
8. *Agreement to refrain from blood donation during the study.*
9. *Provide written informed consent form (ICF).*

Exclusion criteria

1. *Participation in any other COVID-19 prophylactic drug trials during the duration of the study.*
   Note: Participation in COVID-19 treatment trials is allowed in the event of hospitalization due to COVID-19. The study team should be informed as soon as possible.
2. *Positive HIV antibody testing results.*
3. *Participation in SARS-CoV-2 serological surveys where participants are informed of their serostatus during the duration of the study.*
   Note: Disclosure of serostatus post enrolment may accidentally unblind participants to group allocation.
   Participation in this trial can only be allowed if volunteers are kept blinded to their serology results from local/national serological surveys
4. *Planned receipt of any licensed or investigational vaccine, other than the study intervention, within 14 days before and after study vaccination*
5. *Prior receipt of an investigational or licensed COVID-19 vaccine.*
6. *Administration of immunoglobulins and/or any blood products within three months prior to the planned administration of the investigational products (IPs).*
7. *Any confirmed or suspected immunosuppressive or immunodeficient state; positive HIV status; asplenia; recurrent severe infections and chronic use (more than 14 days) of immunosuppressant medication within the past 6 months. Topical steroids or short-term (course lasting ≤14 days) oral steroids are not an exclusion criteria.*
8. *History of allergic disease or reactions likely to be exacerbated by any component of Recombinant COVID-19 vaccine (Sf9 cells)*
9. *Any history of angioedema*
10. *Pregnancy, lactation or willingness/intention to become pregnant within 90 days after receiving study vaccine*
11. *Current diagnosis or treatment of cancer (except basal cell carcinoma of the skin and cervical carcinoma in situ)*
12. *History of serious psychiatric condition likely to affect participation in the study*
13. *Bleeding disorder (e.g. factor deficiency, coagulopathy or platelet disorder), or prior history of significant bleeding or bruising following IM injections or venepuncture*
14. *Suspected or known current alcohol or drug dependency*
15. *Severe and/or uncontrolled cardiovascular disease, respiratory disease, gastrointestinal disease, liver disease, renal disease, endocrine disorder and neurological illness (mild/moderate well-controlled comorbidities are allowed)*
16. *History of laboratory-confirmed COVID-19*
17. *Continuous use of anticoagulants, such as coumarins and related anticoagulants (i.e. warfarin) or novel oral anticoagulants (i.e. apixaban, rivaroxaban, dabigatran and edoxaban)*
18. *Any other significant disease, disorder or finding which may significantly increase the risk to the volunteer because of participation in the study, affect the ability of the volunteer to*

participate in the study or impair interpretation of the study data.

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

Primary Efficacy Endpoint

Virologically confirmed (PCR positive) symptomatic COVID-19 cases first occurring >28 days after completion of 3 doses vaccination, regardless of severity.

Primary Safety Endpoints

1. SAEs from Day 0 through 6 months after completion of 3 doses vaccination.
2. MAAEs from Day 0 through 6 months after completion of 3 doses vaccination.
3. AESIs from Day 0 through 6 months after completion of 3 doses vaccination.
4. Solicited AEs within 7 days after each dose vaccination.
5. Unsolicited AEs within 21 days after the first dose and the second dose, and within 28 days after the third dose vaccination.

Secondary Endpoints

Secondary Efficacy Endpoints

1. Virologically confirmed (PCR positive) symptomatic COVID-19 cases first occurring >14 days after completion of 3 doses vaccination, regardless of severity.
2. Severe COVID-19 and death (based on WHO criteria) caused by SARS-CoV-2 infection first occurring > 14 days after completion of 3 doses vaccination.
3. Severe *COVID-19 and death (based on WHO criteria) caused by SARS-CoV-2 infection first occurring > 28 days after completion of 3 doses vaccination.*
4. *Virologically confirmed (PCR positive) hospitalized moderate, severe COVID-19 and death caused by SARS-CoV-2 infection first occurring > 14 days after completion of 3 doses vaccination.*
5. *Virologically confirmed (PCR positive) hospitalized moderate, severe COVID-19 and death caused by SARS-CoV-2 infection first occurring > 28 days after completion of 3 doses vaccination.*
6. *Serologically confirmed SARS-CoV-2 infection or virologically confirmed (PCR positive) COVID-19 cases first occurring > 14 days after completion of 3 doses vaccination, regardless of symptomatology or severity.*
7. *Serologically confirmed SARS-CoV-2 infection or virologically confirmed (PCR positive) COVID-19 cases first occurring > 28 days after completion of 3 doses vaccination, regardless of symptomatology or severity.*

Secondary Safety Endpoint

SAEs, MAAEs and AESIs from Day 0 through 12 months after completion of 3 doses vaccination in all participants.

Secondary Immunogenicity Endpoints

1. *The seroconversion rate, GMT and GMI of S-RBD IgG antibody on day 28, month 3, month 6 and month 12 after completion of 3 doses vaccination, measured by ELISA.*
2. *The seroconversion rate, GMT and GMI of live-virus neutralizing antibody on day 28, month 3, month 6 and month 12 after completion of 3 doses vaccination.*

Exploratory Endpoints

1. *SARS-CoV-2 virus nucleic acid sequence of COVID-19 cases that occurred > 28 days after completion of 3 doses vaccination derived from isolates or direct NP/OP swab *.*
   ** Note: *Ultra-low temperature preservation of non-inactivated samples or extracted nucleic acids, centralized transportation to*

the central laboratory, unified virus isolation in the P3 laboratory, isolated viruses or non-inactivated samples or extracted nucleic acids shall be arranged by the central laboratory for gene sequencing.

2. *Virologically confirmed (PCR positive) symptomatic COVID-19 cases first occurring >28 days after completion of 3 doses vaccination in different age groups (18-59 group and ≥60 group), regardless of severity.*

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol uji klinik Recombinant COVID-19 Vaccine (Sf9 cells) untuk COVID-19, yang didukung oleh tim ahli melalui rapat pada tanggal 10 Mei 2021, dengan hasil sebagai berikut:

1. Hasil uji non-klinik toksikologi, farmakologi dan *challenge test* pada hewan model mencit, kelinci, dan *Rhesus monkeys*, menunjukan produk yang akan digunakan pada uji klinik memiliki (i) profil keamanan yang masih dapat ditoleransi dengan baik, tidak ditemukan abnormalitas kondisi umum, pemeriksaan fisiologis dan histopatologi organ target; (ii) menginduksi respon imun yang poten, baik humoral maupun seluler, serta memberikan proteksi terhadap keparahan infeksi SARS-CoV-2.
2. Hasil uji klinik fase 1 dan laporan interim fase 2 yang telah dilakukan di China pada subjek dewasa dan lansia, menunjukkan vaksin memiliki profil keamanan yang baik, tidak terdapat efek samping produk uji yang serius. Efek samping produk uji yang terjadi bersifat ringan, baik lokal maupun sistemik. Vaksin bersifat *immunogenic* ditunjukkan dengan peningkatan *seroconversion rate live virus neutralizing antibody* pada 30 hari setelah vaksinasi pada subjek dewasa dan lansia.
3. Desain uji klinik yang diajukan telah memadai.
4. 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.01.06.1.2.07.21.283 tanggal 7 Juli 2021.