RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN SARS-COV-2 MRNA (ARCOV) PRODUKSI
YUXI WALVAX BIOTECHNOLOGY CO., LTD

Informasi Umum

1. Vaksin ARCoV merupakan vaksin SARS-CoV-2 dengan platform mRNA yang dikembangkan oleh **Yuxi Walvax Biotechnology Co., Ltd; Walvax Biotechnology Co., Ltd; dan Suzhou Abogen Biosciences Co., Ltd, China** (sponsor uji klinik). Vaksin ini telah terdaftar *dalam Landscape of Candidate Vaccines in Clinical Development WHO.*
2. Tersedia uji non klinik untuk imunogenisitas (netralisasi antibodi) pada mice, uji imunogenisitas dan toksisitas pada *Cynomolgus Monkeys*, uji tantang, uji anafilaksis, dan uji *local muscle irritation*.
3. Tersedia hasil uji klinik fase I yang menunjukkan vaksin dapat ditoleransi dengan baik . Hasil uji klinik fase II telah menentukan dosis vaksin yaitu 15 mcg.

Informasi Uji Klinik

1.	Judul protokol	:	***A Global, Multi-center, Randomized, Double-Blind, Placebo-controlled, Phase III Clinical Study to Evaluate the Protective Efficacy, Safety and Immunogenicity of SARS-CoV-2 Messenger Ribonucleic Acid (mRNA) Vaccine in Population Aged 18 Years and Older*** *Protocol No. ARCoV-005 version 2.0 dated Jun 29, 2021*
2.	Produk Uji	:	Vaksin SARS-CoV-2 mRNA (ARCoV). Vaksin diberikan 2 (dua) kali pada hari ke-0 dan hari ke-28 secara intramuskular. Produsen: Yuxi Walvax Biotechnology Co., Ltd., China
3.	Produk Pembanding	:	Placebo dari vaksin SARS-CoV-2 mRNA (ARCoV). Vaksin diberikan 2 (dua) kali pada hari ke-0 dan hari ke-28 secara intramuskular.
4.	Center/ Peneliti	:	Produsen: Yuxi Walvax Biotechnology Co., Ltd., China Rumah Sakit Umum Pusat Persahabatan, Jakarta/ Dr. dr. Erlina Burhan, MSc, Sp.P(K) *Satellite Site:* RSPI Sulianti Saroso, Puskesmas Cilincing, Puskesmas Pulogadung, Puskesmas Ciracas, Puskesmas Duren Sawit, Puskesmas Cakung, Puskesmas Kalideres, dan Puskesmas Kebayoran Lama
5.	Sponsor/ ORK	:	PT. Etana Biotechnologies Indonesia / PT. Tigermed Consulting Indonesia
6.	Persetujuan Etik	:	Persetujuan Komite Etik No. 71.A/KEPK-RSUP/08/2021 tanggal 10 Agustus 2021 dari Komite Etik Penelitian Kesehatan Rumah Sakit Persahabatan
7.	Desain Uji Klinik	:	*Global multicenter, randomized, double-blind, placebo-controlled, parallel-group clinical study design to evaluate the protective efficacy, safety and immunogenicity of the investigational vaccine in adults aged 18 years or older.*
8.	Jumlah subjek	:	28.000 subject
9.	Tujuan uji klinik	:	***Primary objective*** ***Protective Efficacy:*** *To evaluate the protective efficacy of the SARS-CoV-2 mRNA vaccine in the prevention of COVID-19 (refer to Appendix 1) starting from at least 14 days (≥D42) after the two-dose immunization (with an interval of 28 days) in subjects aged 18 years and older.*

Safety:
To evaluate the safety and reactogenicity of the SARS-CoV-2 mRNA vaccine after the two-dose immunization (with an interval of 28 days) in subjects aged 18 years and older

Secondary objectives
Protective Efficacy

1. *To observe the protective efficacy of the SARS-CoV-2 mRNA vaccine in the prevention of severe and critical COVID-19 (refer to Appendix 1) starting from at least 14 days (≥D42) after the two-dose immunization (with an interval of 28 days) in subjects aged 18 years and older;*
2. *To observe the protective efficacy of the SARS-CoV-2 mRNA vaccine in the prevention of COVID-19 leading to death (refer to Appendix 1) starting from at least 14 days (≥D42) after the two-dose immunization (with an interval of 28 days) in subjects aged 18 years and older;*
3. *To observe the protective efficacy of the SARS-CoV-2 mRNA vaccine in the prevention of COVID-19 (refer to Appendix 1) starting from at least 14 days (≥D14) after the first vaccination in subjects aged 18 years and older.*

Safety
To observe the serious adverse events (SAEs) and adverse events of special interest (AESIs) from the first vaccination through 12 months after two-dose immunization in a population aged 18 years and older.

Exploratory objectives:

1. *To observe the seroconversion rate, geometric mean titer (GMT) and geometric mean increase (GMI) of SARS-CoV-2 S-RBD specific IgG antibody at day 14, day 28, month 3, month 6 and month 12 after two-dose immunization among subjects in the immunogenicity subgroup;*
2. *To observe the seroconversion rate, geometric mean titer (GMT) and geometric mean increase (GMI) of anti-SARS-CoV-2 pseudovirus neutralizing antibody at day 14, day 28, month 3, month 6 and month 12 after two-dose immunization among subjects in the immunogenicity subgroup;*
3. *To observe the seroconversion rate, geometric mean titer (GMT) and geometric mean increase (GMI) of anti-SARS-CoV-2 euvirus neutralizing antibody at day 14, day 28, month 3, month 6 and month 12 after two-dose immunization among subjects in the immunogenicity subgroup.*

10. Kriteria Eligibilitas :

Inclusion Criteria:
The subjects must meet all of the following inclusion criteria:

1. *Adults aged 18 years and older, male and female;*
2. *Understanding the contents of the informed consent form and information of this clinical study, and be willing to and able to sign the informed consent form;*
3. *Be able to well communicate with the investigator, and to understand and comply with the requirements of this clinical study;*
4. *Being at risks of infection with or exposure to SARS-CoV-2 or COVID-19 due to factors such as regions, occupation, activities, environment etc.*
5. *For female subjects: having no childbearing potential or having used effective methods of contraception within 2 weeks prior to enrollment into this study, having a negative pregnancy test.*

No childbearing potential includes amenorrhea for at least 1 year or medical record documented surgical sterilization. Subjects voluntarily agree to continue using effective contraceptive methods until 3 months after the fourth dose. The effective contraceptive methods include sexual abstinence or adequate contraceptive methods such as intrauterine or implanted contraceptive device, oral contraceptives, injected or implanted contraceptives, sustained-release topical contraceptives, intrauterine device (IUD), condoms (male), diaphragm, and cervical cap, etc.;

6. *Healthy subjects or subjects with mild underlying diseases [in a stable status that the disease does not worsen (requiring no hospitalization for treatment or no major adjustment of treatment regimens) for at least 3 months prior to enrollment into this study].*

Exclusion Criteria

Exclusion criteria for the first dose

Subjects meeting any of the following exclusion criteria are not allowed to be enrolled:

1. *Medical history of COVID-19 or prior use of any medications to prevent COVID-19 (e.g., history of vaccination against any SARS-CoV-2 vaccine, marketed or not marketed);*
2. *Positive results of SARS-CoV-2 etiological testing (RT-PCR Assay) (subjects with serological testing showing positive IgG antibody and/or IgM antibody can be enrolled);*
3. *Prior medical history of severe acute respiratory syndrome (SARS), middle east respiratory syndrome (MERS) and other human coronavirus infections or diseases;*
4. *Fever (oral temperature≥37.5°C/ axillary temperature≥37.3°C) on the day of the first vaccination or within recent 72 hours;*
5. *Pregnant (e.g., positive pregnancy test) or breastfeeding women;*
6. *Plan of pregnancy or interruption of effective contraceptive methods within 3 months after the fourth vaccination in this study;*
7. *Personnel of the study institution or sponsor;*
8. *Prior history of allergic reaction or anaphylaxis to any vaccine or drug, e.g., hypersensitivity, urticaria, serious eczema, difficulty breathing, laryngeal edema, and angioedema etc.;*
9. *Have inoculated or planned to inoculate with any vaccines other than the vaccines used in this clinical study from 28 days prior to the first vaccination to 28 days after the fourth vaccination in this study (except "vaccines for emergency" such as tetanus vaccine or rabies vaccine);*
10. *Have participated in or planned to participate in clinical studies of other drugs from 28 days prior to the first vaccination to 12 months after the fourth vaccination in this study;*
11. *Hereditary hemorrhagic tendency or coagulation dysfunction (e.g., cytokine defects, coagulation disorders or platelet disorder), or a history of significant bleeding, or a history of intramuscular injection or venipuncture injury;*
12. *Known medical history or diagnosis confirming that subjects have diseases affecting immune system function, including cancer (except skin basal cell carcinoma), congenital or acquired immunodeficiency (e.g., infection with human immunodeficiency virus (HIV)), uncontrolled autoimmune disease;*
13. *Asplenia or functional asplenia;*
14. *Long-term use (continuous use ≥14 days) of immunosuppressants or other immunomodulators (e.g., glucocorticoids: prednisone or similar drugs) within 6 months prior to the first vaccination in this study, except for topical*

medications (e.g., ointments, eye drops, inhalants or nasal sprays). However, the topical medications should not exceed the recommended dose in the package insert or induce any signs of systemic exposure;

15. *Having received immunoglobulins and/or blood products within 3 months prior to the first vaccination in this study;*
16. *Suspected or known alcohol dependency or drug abuse, which may affect safety evaluation or subject's compliance;*
17. *Planning to permanently move from the local area before study completion or leave the local area for a long time during the period of study visits;*
18. *Other circumstances considered by the investigator as inappropriate to participate in the study.*

11. Luaran Uji Klinik/ Endpoint :

Primary Protective Efficacy Endpoint:

The person-year incidence rate of COVID-19 starting from at least 14 days (≥D42) after the two-dose immunization in subjects aged 18 years and older;

Secondary Protective Efficacy Endpoints:

1. *Person-year incidence rate of severe and critical COVID-19 starting from at least 14 days (≥D42) after the two-dose immunization in subjects aged 18 years and older;*
2. *Person-year incidence rate of COVID-19 resulting in death starting from at least 14 days (≥D42) after the two-dose immunization in subjects aged 18 years and older;*
3. *Person-year incidence rate of COVID-19 starting from at least 14 days (≥D14) after the first vaccination in subjects aged 18 years and older;*

Primary Safety Endpoints:

1. *incidence rates of adverse events within 28 days after the first and second vaccination among all subjects;*
2. *incidence rates of solicited adverse events (AEs) within 30minutes, 7 days after the first and second vaccination among subjects in reactogenicity subgroup;*

Secondary Safety Endpoints:

The incidence rates of SAEs and AESIs from the first vaccination through 12 months after the two-dose immunization among all subjects.

Exploratory Endpoints:

1. *To observe the SARS-CoV-2 S-RBD specific IgG antibody level at day 14, day 28 month 3, month 6 and month 12 after two-dose immunization among subjects in the immunogenicity subgroup;*
2. *To observe the anti-SARS-CoV-2 pseudovirus neutralizing antibody titer at day 14, day 28, month 3, month 6 and month 12 after two-dose immunization among subjects in the immunogenicity subgroup;*
3. *To observe the anti-SARS-CoV-2 euvirus neutralizing antibody titer at day 14, day 28, month 3, month 6 and month 12 after two-dose immunization among subjects in the immunogenicity subgroup;*
4. *SARS-CoV-2 sequencing of COVID-19 cases occurred 14 days after one-dose immunization schedule.*

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol uji klinik Vaksin SARS-COV-2 mRNA (ARCOV) yang didukung oleh tim ahli melalui rapat pada tanggal 7 Agustus 2021. Berdasarkan hasil uji non klinik untuk uji imunogenisitas, uji tantang dan uji toksisitas, vaksin dapat ditoleransi dengan baik dan menghasilkan respon imun antibodi (IgG dan netralisasi antibodi) setelah pemberian suntikan pertama dan meningkat pada suntikan kedua. Desain uji klinik yang diajukan telah memadai. 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.01.06.1.3.08.21.76 tanggal 27 Agustus 2021.