RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN ZF2001
PRODUKSI ANHUI ZHIFEI LONGCOM BIOPHARMACEUTICAL CO.LTD

Informasi Umum

1. Vaksin ZF2001 merupakan *Recombinant Novel Coronavirus Vaccine* (CHO cell) yang diproduksi oleh Anhui Zhifei Longcom Biopharmaceutical Co., Ltd. Vaksin dengan platform subunit ini telah terdaftar dalam WHO *Draft Landscape* of COVID-19 Candidate Vaccine.
2. Uji klinik fase III yang diajukan telah didukung oleh uji non-klinik toksikologi, farmakologi dan *challenge test* pada hewan model tikus, kelinci, tikus belanda, dan makaka. Uji klinik fase I dan fase II telah dilaksanakan di China.
3. Uji klinik fase III yang diajukan direncanakan dilakukan multicenter di China, Uzbekistan, Pakistan, Ekuador dan Indonesia.

Informasi Uji Klinik

1.	Judul Protokol	:	***A Phase III Randomized, Double-blind, Placebo-controlled Clinical Trial in 18 Years of Age and Above to Determine the Safety and Efficacy of ZF2001, a Recombinant Novel Coronavirus Vaccine (CHO Cell) for Prevention of COVID-19*** No. protokol LKM-2020-NCV-GJ01, Versi 1.1, 28 November 2020
2.	Produk Uji	:	*Novel Coronavirus Spike Protein - Receptor Binding Domain* (NCP RBD) dari SARS-COV-2 *Spike Protein* (25µg) dan *adjuvant* aluminum hydroxide (0,25 mg) dalam 0.5 ml, diberikan 3 kali pada bulan ke-0, 1, dan 2 secara intramuskular Produsen : Anhui Zhifei Longcom Biopharmaceutical Co.
3.	Produk Pembanding	:	Aluminum hydroxide (0.25 mg) dalam 0,5 ml, diberikan 3 kali pada bulan ke-0, 1, dan 2 secara intramuskular Produsen : Anhui Zhifei Longcom Biopharmaceutical Co.
4.	Center/Peneliti	:	1. Departemen Ilmu Kesehatan Anak FKUI-RSCM, Jakarta/Prof. Dr. dr. Hindra Irawan Satari, Sp.A(K), M.Trop Paed *Satellite site*: Puskesmas Kec. Senen, Puskesmas Kec. Koja, Puskesmas Kec. Tambora, Puskesmas Kec. Pasar Minggu, Puskesmas Kec. Jatinegara, Puskesmas Kec. Cempaka Putih, Puskesmas Kec. Cilincing, Puskesmas Kec. Cengkareng, Puskesmas Kec. Pesanggrahan, Puskesmas Kec. Kramat Jati 2. Departemen Ilmu Kesehatan Anak FK UNPAD-RSHS, Bandung/dr. Rodman Tarigan, Sp.A (K), M.Kes *Satellite site*: RSUP dr. Hasan Sadikin, RS Immanuel, RS Limijati, RS Advent Bandung, RS Al-Ihsan, RSIA Kota Bandung, RS Unggul Karsa Medika
5.	Sponsor / ORK	:	Anhui Zhifei Longcom Biopharmaceutical Co., Ltd / PT. Prodia DiaCRO Laboratories
6.	Persetujuan Etik	:	1. No. KET-1492/UN2.F1/ETIK/PPM.00.02/2020 tanggal 28 Desember 2020 dari Komisi Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Indonesia – RSUPN Dr. Cipto Mangunkusumo Jakarta 2. No. LB/02/01/X.6.5/13/2021 tanggal 21 Januari 2021 dari Komisi Etik Penelitian Kesehatan RSUP Dr. Hasan Sadikin Bandung

7.	Desain Uji Klinik	:	*A randomized, double-blind, placebo-controlled, international multicenter clinical trial design will be adopted. Efficacy, immunogenicity, and safety will be evaluated. Screening eligible subjects will be 1:1 randomly assigned to the experimental group and the placebo control group, and vaccinated as per the 0, 1, 2 month immunization schedule. 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.*
9.	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.*
10.	Tujuan Uji Klinik	:	***Primary Objective*** *To evaluate the efficacy and safety of the Recombinant Novel Coronavirus Vaccine (CHO Cell) against any severity of COVID-19 in a population aged 18 years and above.* ***Secondary Objectives*** *1. To evaluate the efficacy of the Recombinant Novel Coronavirus Vaccine (CHO Cell) against the severity of severe and above COVID-19 in a population aged 18 years and above.* *2. To evaluate the immunogenicity and immune persistence of the Recombinant Novel Coronavirus Vaccine (CHO Cell) in a population aged 18 years and above.* *3. To evaluate the efficacy of the Recombinant Novel Coronavirus Vaccine (CHO Cell) as emergency vaccination against any severity of COVID-9 in a population aged 18 years and above.* *4. To evaluate the efficacy of the Recombinant Novel Coronavirus Vaccine (CHO Cell) against any severity of COVID-9 in populations of different age group (18-59 years vs. 60 years and above).* ***Exploratory objectives*** *To explore the immunological surrogate variables of the Recombinant Novel Coronavirus Vaccine (CHO Cell) against COVID-19 in a population aged 18 years and above.*
11.	Kriteria Eligibilitas	:	***Inclusion criteria*** *1. Population aged ≥18 years old;* *2. Subjects voluntarily participate in the study and sign the informed consent form; and are able to provide valid identification, and understand and comply with the requirements of the trial protocol;* *3. Female subjects of childbearing age agree to use effective contraceptive measures from the beginning of the study to 2 months after full course of vaccination.* ***Exclusion criteria*** *1. Suspected or confirmed as fever(axillary temperature ≥37.3°C / oral temperature ≥37.5°C) within 72 hours before the enrollment, or axillary temperature ≥37.3°C / oral temperature ≥37.5°C at the day of screening;* *2. Diastolic blood pressure ≥ 100 mmhg and / or systolic blood pressure ≥ 150 mmhg;* *3. Patients with previous history of a COVID-19;*

4. *Detection of SARS-COV-2 nucleic acid or antibody is positive(in Indonesia, detection ofSARS-COV-2 antigen or antibody is positive);*
5. *Those who are suffering from the following diseases:*
   a. *With thrombocytopenia, any coagulation dysfunction or receiving anti-coagulatory treatment*
   b. *Congenital or acquired immune deficiency or autoimmune disease history; no spleen, or history of splenic surgery and trauma, or receiving immunomodulator treatment within 6 months, e.g., immunosuppressive dose of glucocorticoids (reference dose: equivalent to 20mg/ day of prednisone, over 1 week); Or monoclonal antibodies; Or thymosin; Or interferon etc.; However, topical application (such as ointment, eye drops, inhalers or nasal sprays) is permitted;*
   c. *Symptoms related to acute respiratory tract infection (such as sneezing, nasal congestion, runny nose, cough, sore throat, loss of taste, chills, shortness of breath, etc.);*
   d. *Cancer patients (except basal cell carcinoma)*
6. *With a history of serious allergy to any vaccine or any composition of Investigational product (including: aluminum preparations), such as allergic shock, allergic throat edema, allergic purpura, thrombocytopenic purpura, localized allergic necrosis reaction (Arthus reaction), dyspnea and angioneuroedema;*
7. *Inoculated with subunit vaccine and inactivated vaccine within 14 days before the first dosing of investigational? vaccine, or inoculated with attenuated live vaccine within 30 days;*
8. *Previous receiving blood transfusion or blood relevant products (including immunoglobulin) within 3 months, or planning to receive such products from the starting of study to <6 months after the whole-course inoculation;*
9. *Have participated in or are participating in other covid-19 related clinical trials;*
10. *Women in breastfeeding period or in pregnant period (including women at childbearing age with positive result of urine pregnancy test);*
11. *Considered by investigators as any disease or state possibly making the subject at unacceptable risk; not conforming to the requirements of study protocol; interference of assessment of reactions of vaccine.*

12. *Endpoint* Uji Klinik : ***Primary Endpoints:***
    1. *The number of any severity of COVID-9 cases 14 days after whole vaccination.*
    2. *The endpoint of safety study:*
       a. *Analysis of adverse events from the first dose of vaccination until 30 days after full course of vaccination: incidence of adverse reactions or adverse events; incidence of grade 3 or above adverse reactions or adverse events; incidence of adverse reactions or adverse events leading to withdrawal.*
       b. *Analysis of serious adverse events from the first dose of vaccination until 12 months after full course of vaccination: incidence of serious adverse events; incidence of serious adverse events associated with Investigational product.*

Secondary endpoints:

1. *The endpoint of efficacy study:*
   a. *The number of severe and severity above COVID-19 cases 14 days after whole vaccination;*
      The number of any severity of COVID-9 cases after first dose of vaccination;
   b. *The number of COVID-19 cases of any severity in populations of different age group (18-59 years vs. 60 years and above) 14 days after whole vaccination.*
2. *Endpoint of immunogenicity and immune persistence study:*
3. *The level of neutralizing antibody to SARS-COV-2 and IgG level of RBD protein binding antibody at 14 days and 6 months after full course of vaccination.*

Exploratory endpoint:

The protective level of neutralizing antibody to SARS-COV-2 and IgG of RBD protein binding antibody against COVID-19 caused by SARS-COV-2 infection.

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol uji klinik vaksin ZF2001 untuk COVID-19, yang didukung oleh tim ahli melalui rapat pada tanggal 12 Desember 2020 dengan hasil sebagai berikut:

1. Hasil uji non-klinik toksikologi, farmakologi dan *challenge test* pada hewan model tikus, kelinci, tikus belanda, dan macaca dengan dosis yang setara yang akan digunakan pada manusia menunjukkan produk yang akan digunakan dalam uji klinik memiliki (i) profil keamanan yang masih dapat ditoleransi dengan baik (ii) imunogenisitas yang baik dan menginduksi imunitas terhadap infeksi SARS-CoV-2 pada hewan model.
2. Uji klinik fase 1 dan 2 di China memberikan hasil seluruh parameter *preliminary* imunogenisitas meningkat (*positive conversion rate live virus neutralizing antibody, GMT live virus neutralizing antibody, positive conversion rate RBD protein binding antibody dan GMT RBD protein binding antibody*) seiring dengan penambahan pengulangan penyuntikan. Hasil studi *preliminary* keamanan menunjukkan tidak terdapat efek samping produk uji serius. Sebagian besar efek samping produk uji bersifat ringan (grade 1 dan 2) dan dapat teratasi.
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.01.06.1.3.02.21.07 tanggal 3 Februari 2021.