RINGKASAN HASIL EVALUASI PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK (PPUK) FASE 2 VAKSIN SARS-CoV-2 (VERO CELL) *INACTIVATED* PRODUKSI BEIJING BIO-INSTITUTE-BIOLOGICAL PRODUCTS CO., LTD CHINA SEBAGAI VAKSIN *BOOSTER* PADA DEWASA

Informasi Umum

1. Vaksin SARS-CoV-2 (Vero cell) *Inactivated* diproduksi oleh Beijing Bio-Institute-Biological Products Co., Ltd China dan didaftarkan oleh PT Kimia Farma telah mendapat *Emergency Use Authorization* (EUA) dari Badan POM sebagai vaksin primer pada dewasa di atas 18 tahun.
2. Hasil uji klinik akan digunakan sebagai data dukung penambahan posologi dan indikasi Uji klinik yang diajukan ditujukan untuk mendapatkan data pendukung penambahan posologi dan indikasi vaksin sebagai *booster* terhadap vaksin primer (Vaksin SARS-CoV-2 (Vero cell) *Inactivated*; CoronaVac, Cominarty dan Vaxzevria.

Informasi Uji Klinik

1.	Judul Protokol	:	***A Phase II Non-Randomized Open Labelled Clinical Trial to Evaluate the Safety & Immunogenicity of SARS-COV-2 Vaccine (Vero Cell) Inactivated as A Booster Dose.*** *BOOST-VC-0221 Version 2.0 tanggal 15 Desember 2021*
2.	Nama Produk Uji	:	*SARS-COV2 Vaccine (Vero Cell) Inactivated* 4 mcg (6,5 U) diberikan 1 kali secara intramuscular.
3.	Peneliti Utama	:	dr. Prenali Dwisthi Sattwika, Sp.PD
4.	Center/Peneliti	:	1. Rumah Sakit JIH, D.I. Yogyakarta / dr. Deshinta Putri Mulya, Sp.PD-KAI 2. RSUD dr. Saiful Anwar Malang, Jawa Timur / dr. Muhammad Anshory, Sp.PD 3. RSUD Ulin Banjarmasin, Kalimantan Selatan / dr. Nanang Miftah Fajari, Sp.PD-KEMD 4. Rumah Sakit Universitas Udayana, Bali / dr. Cokorda Wahyu Purnamasidhi, M.Biomed., Sp.PD 5. RSUD Bali Mandara, Bali / dr. I Ketut Agus Somia, Sp.PD 6. Klinik dan Laboratorium Kimia Farma Diponegoro, Bandung, Jawa Barat / dr. Dewi Rinakanti, Sp. PK 7. Klinik dan Laboratorium Kimia Farma Radio Dalam, Jakarta / dr. Andi Wiradharma, Sp. PK 8. Klinik dan Laboratorium Kimia Farma Sutomo Semarang, Jawa Tengah / Dr. dr. I. Edward KSL, MM, MHKes, SpPK(K), MSi.Med 9. Klinik dan Laboratorium Kimia Farma Adisucipto, D.I. Yogyakarta / dr. Nuur Naafi Ulloh, M.Sc, Sp.PK
5.	Sponsor	:	PT. Kimia Farma
6.	Persetujuan Etik	:	No. KE/FK/1340/EC/2021 tanggal 14 Desember 2021 untuk protokol versi 1.4 tanggal 22 November 2021 dari Komite Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Gadjah Mada.
7.	Desain Uji Klinik	:	*This is a phase 2, non-randomized, open-label, clinical trial to evaluate the safety of SARS-COV-2 Vaccine (Vero Cell) Inactivated up to 6*

months post booster dose and immunogenicity up to 12 months post booster dose in adults aged 18 years old and above who have received the 2 prime doses of one of SARS-COV-2 Vaccines (Vero Cell inactivated-Sinopharm SARS-COV-2 Vaccine, CoronaVac SARS-COV-2 Vaccine, AstraZeneca SARS-COV-2 Vaccine, or Cominarty/Pfizer mRNA COVID-19 Vaccine) authorized for emergency use (EUA) in Indonesia.

8. Jumlah Subjek : *The sample calculation for this trial is based on the following assumptions based on a sample size calculation for before-after study (Chow et al., 2008; Rosner, 1995) using immunogenicity data as follows:*
   1) The minimum clinical difference to detect is 1.75 folds of GMT of anti-sRBD IgG and/or Neutralizing Antibody for pre and post intervention at 0.243 on log scale (base 10).
   2) The standard deviation of the GMT of anti-sRBD IgG and/or Neutralizing Antibody pre and post intervention on log scale (base 10) is 1.0 (assumed population standard of 2.0 and within-subject correlation of 0.875).

   Based on assumption above, this trial will need to recruit 178 participants in each study arm to achieve 80% power at two-sided 5% significance level. Anticipating 10% of drop-out participants, we expanded to approximately 200 participants per vaccine.

9. Tujuan Uji Klinik : *Primary objective*
   1. *To evaluate the immunogenicity at 14 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated in participants who had received second dose of SARS-CoV-2 prime vaccine between 6 to 12 months compared to baseline.*
   2. *To evaluate the immunogenicity at 28 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated in participants who had received second dose of SARS-CoV-2 prime vaccine between 6 to 12 months compared to baseline.*

   Secondary objective
   1. *To evaluate the immunogenicity among participants who had received second dose of SARS-CoV-2 prime vaccine between 6 to 12 months compared to baseline at:*
      a) 90 days after one booster dose 0.5 mL intramuscular (IM) injection of SARSCOV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.
      b) 180 days after one booster dose 0.5 mL intramuscular (IM) injection of SARSCOV-2 Vaccine (Vero Cell) Inactivated-Sinopharm.
      c) 360 days after one booster dose 0.5 mL intramuscular (IM) injection of SARSCOV-2 Vaccine (Vero Cell) Inactivated – Sinopharm from baseline among Sinopharm
   2. *To evaluate the safety profile of one booster dose 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated in participants who*

had received second dose of SARSCoV-2 prime vaccine between 6 to 12 months.

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

1. *Adult males or females aged 18 years and above at the time of consent.*
2. *Participants who provide a voluntarily consent to participate in the study and sign the consent form.*
3. *Participants who have previously received homologous 2-dose of SARS-COV-2 Vaccine (either Vero Cell inactivated-Sinopharm SARS-COV-2 Vaccine, CoronaVac SARSCOV-2 Vaccine, AstraZeneca Vaccine, or Cominarty/Pfizer mRNA COVID-19 Vaccine) authorized for emergency use, between 6 to 12 months post second prime vaccine dose prior to Day 1.*
4. *Participants who have negative results for swab SARS-COV-2 rapid antigen test.*

Kriteria Eksklusi / *Exclusion criteria*

1. *Participants who are unable to follow clinical and follow-up procedures.*
2. *Participants with acute fever with temperature above 38℃, coughing, breathing difficulty, chills, muscle ache, headache, sore throat, loss of smell, or loss of taste within 72 hours prior to the dosing.*
3. *Participants with a history of PCR-confirmed SARS-CoV-2 infection in the last 90 days prior to dosing.*
4. *Female who are pregnant or breastfeeding.*
5. *Participants with a history of hypersensitivity or allergic reactions including anaphylaxis.*
6. *Participants with immune dysfunction, including immunodeficiency disorder, or family history of such conditions, except HIV-positive participants in stable/well-controlled condition.*
7. *Participants who received chronic administration (defined as more than 14 continuous days) of immunosuppressant medication such as immunomodulator, immune-modifying drug, immunoglobulin, immunotherapy, chemotherapy, systemic corticosteroid, etc. except topical steroids or short-term oral steroids (course lasting 14 days), or blood-derived products in the last 90 days prior to dosing.*
8. *Participants with a current clinically significant chronic and unstable cardiovascular,endocrine, gastrointestinal, hepatic (including hepatitis B and C), renal, neurological, respiratory, psychiatric or other medical disorders not excluded by other exclusion criteria, that are assessed by the investigator as being clinically unstable within the prior 90 days as evidenced by:*
   a) *Hospitalization for the condition, including day surgical interventions*
   b) *New significant organ function deterioration*
   c) *Needing addition of new treatments or major dose adjustments of current treatments (mild or moderate well-controlled comorbidities are allowed)*
9. *Participants with hemophilia or people using anticoagulants who are at a risk of serious bleeding from IM injection.*
10. *Participants with a current dependent on antipsychotic drugs and narcotic analgesics, or suspected of alcohol or drug dependency.*

11. *Participants who have received or plans to receive other vaccination(s) within 28 days prior to or during study duration (except for influenza vaccine which is not allowed within 14 days before, or 4 weeks after final dose of IP).*
12. *Participants who have received or have plans to receive other investigational drug(s) while participating in another clinical study or bioequivalence study within 28 days prior to vaccination.*

11. Luaran Uji Klinik : *Primary Endpoints*:

1. *Geometric Mean Titer (GMT) of anti-SARS-CoV-2 neutralizing antibody at:*
   a) *Preadiministration of 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   b) *14 days after one booster 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   c) *28 days after one booster 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
2. *Geometric Mean Fold Rise (GMFR) of anti-SARS-CoV-2 neutralizing antibody at :*
   a) *Preadiministration of 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   b) *14 days after one booster 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   c) *28 days after one booster 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
3. *GMT of anti-spike Receptor Binding Domain (sRBD) IgG antibody at:*
   a) *Preadiministration of 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   b) *14 days after one booster 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   c) *28 days after one booster 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
4. *GMF of anti-spike Receptor Binding Domain (sRBD) IgG antibody at:*
   a) *Preadiministration of 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   b) *14 days after one booster 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   c) *28 days after one booster 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*

Secondary Endpoints:

1. *GMT of of anti-SARS-CoV-2 neutralizing antibody at:*
   a) *90 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   b) *180 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   c) *360 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV2 Vaccine (Vero Cell) Inactivated – Sinopharm.*

2. *GMFR of of anti-SARS-CoV-2 neutralizing antibody at :*

a) *90 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
b) *180 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
c) *360 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*

3. *GMT of anti-sRBD IgG antibody at :*
   a) *90 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   b) *180 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   c) *360 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV2 Vaccine (Vero Cell) Inactivated– Sinopharm.*
4. *GMFR of anti-sRBD IgG antibody at :*
   a) *90 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   b) *180 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
   c) *360 days after one booster dose 0.5 mL intramuscular (IM) injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated – Sinopharm.*
5. *Proportions of solicited adverse events within 7 days after one booster dose 0.5 mL IM injection of investigational product in participants who had received second dose of SARSCoV-2 prime vaccine at least 6 months.*
6. *Proportions of unsolicited adverse events within 28 days after one booster dose 0.5 mL IM injection of investigational product in participants who had received second dose of SARSCoV-2 prime vaccine at least 6 months.*
7. *Proportions of clinically significant abnormal liver function (AST, ALT, Total Bilirubin) at 14 days and 28 days after one booster dose 0.5 mL IM injection of investigational product.*
8. *Proportions of serious adverse events within 180 days after one booster dose 0.5 mL IM injection of SARS-COV-2 Vaccine (Vero Cell) Inactivated in participants who had received second dose of SARS-CoV-2 prime vaccine at least 6 months.*

Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol uji klinik untuk VAKSIN SARS-CoV-2 (VERO CELL). Hasil evaluasi telah didukung tim ahli melalui rapat pada 9 November 2021 dengan hasil sebagai berikut:

1. Vaksin uji telah mendapatkan EUA sebagai vaksin primer untuk dewasa di atas 18 tahun dari Badan POM pada 27 Januari 2022.
2. Desain uji klinik yang diajukan telah memadai termasuk
3. Vaksin uji yang akan digunakan telah memenuhi persyaratan mutu.

Keputusan

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik No. PP.01.05.1.12.21.493 tanggal 28 Desember 2021