RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN PNEUMINVAC
(13-VALENT PNEUMOCOCCAL POLYSACCHARIDE CONJUGATE VACCINE (TT/DT)
PRODUKSI BEIJING MINHAI BIOTECHNOLOGY CO., LTD.

Informasi Umum

1. Vaksin Pneuminvac telah mendapatkan nomor izin edar di Indonesia tanggal 25 Oktober 2023. Uji klinik yang diajukan adalah uji klinik fase 3 untuk pemberian Vaksin Pneuminvac bersama dengan Vaksin Hexavalent (Pneuminvac pada bayi pada usia 2, 4 dan 12-15 dan Vaksin Hexavalent pada bayi usia 2, 3 dan 4 bulan).
2. Selain itu, uji klinik akan menggunakan regimen dosis yang berbeda dengan posologi yang disetujui BPOM. Hal ini untuk menyesuaikan regimen dosis yang direkomendasikan WHO yang telah diadopsi ke dalam program vaksinasi nasional.

Informasi Uji Klinik

1.	Judul Protokol	:	*A Multi-center, Randomized, Blinded, Active-controlled, Phase 3 Clinical Study to Evaluate the Immunogenicity and Safety of 13-valent Pneumococcal Polysaccharide Conjugate Vaccine Co-administered with Hexavalent Vaccine at 2, 4 and 12-15 Months of Age to Health Infants in Indonesia* (versi 1.0, 25 Juni 2024)
2.	Produk Uji	:	Pneuminvac® (*13-valent Pneumococcal Polysaccharide Conjugate Vaccine (TT/DT)*) 3 kali secara intramuskular Produsen: Beijing Minhai Biotechnology Co., Ltd.
3.	Produk Pembanding	:	Prevenar 13® (*Pneumococcal 13-valent conjugate vaccine*) 3 kali secara intramuskular Produsen: Pfizer Ireland Pharmaceuticals
4.	Center / Peneliti	:	1. Program Studi Magister Ilmu Kesehatan Masyarakat Fakultas Kedokteran Universitas Udayana *Fieldsite:* Puskesmas I Denpasar Selatan dan Puskesmas II Denpasar Utara 2. Departemen Ilmu Kesehatan Anak Fakultas Kedokteran Universitas Padjadjaran/ RSUP dr. Hasan Sadikin Bandung *Fieldsite*: Puskesmas Garuda, Puskesmas Ciumbuleuit, Puskesmas Dago
5.	Sponsor / ORK	:	Beijing Minhai Biotechnology Co., Ltd / PT. Prodia Diacro Laboratories
6.	Persetujuan Etik	:	1. No. 1928/UN14.2.2.VII.14/LT/2024 tanggal 22 Agustus 2024 Komisi Etik Penelitian Fakultas Kedokteran Universitas Udayana 2. No. 955/UN6.KEP/EC/2024 tanggal 28 Agustus 2024 dari Komite Etik Penelitian Fakultas Kedokteran Universitas Padjadjaran
7.	Desain Uji Klinik	:	*A multicenter, randomized, blinded, active-controlled Phase III study. The participants who are enrolled in the study group will receive study PCV13 vaccine and co-administered with hexavalent vaccine; control group will receive Pfizer PCV13 vaccine (Prevenar13®) and co-administered with hexavalent vaccine.*
8.	Jumlah Subjek	:	*A total of approximately 500 infants 6-8 weeks of age (WOA) will be enrolled and randomized in 1:1 ratio into the study group and control group, with 250 participants in each group.*
9.	Tujuan Uji Klinik	:	*Primary Objective* *To evaluate the serotype-specific IgG responses 30 days after booster dose of the investigational vaccine.*

Secondary Objective

- *To assess the solicited AEs (local and systemic) occurring 0-7 days after each dose of the investigational vaccine.*
- *To assess the unsolicited AEs occurring 0 - 30 days after each dose of the investigational vaccine*
- *To assess SAE from 1st dose to 6 months after booster dose of the investigational vaccine.*
- *To evaluate the serotype-specific IgG responses 30 days after 2nd dose of the investigational vaccine.*
- *To evaluate the serotype-specific Opsonophagocytic Activicity (OPA) 30 days after the 2nd dose, before the booster dose, and 30 days after the booster dose of the investigational vaccine in OPA subgroup.*
- *To evaluate the immune responses induced by hexavalent vaccine 30 days after the 2nd dose of the investigational vaccine in different subsets.*

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

1. *Healthy infants based on medical history and clinical assessment.*
2. *Infants age of 6-8 weeks at enrolment. Infants will be eligible since the day they reach 6 weeks of age and until 8 weeks of age included.*
3. **Body weight at enrollment ≥3.0 kg (If the subject does not meet the criteria, the visit may be rescheduled when the criteria is met.).*
4. **On the day of vaccination and within 3 days prior to 1st dose of vaccination, axillary temperatures <37.5^{0}C/99.1^{0}F (If the subject does not meet the criteria, the visit may be rescheduled when the criteria is met.).*
5. *Infant's parent(s) or legal guardian must be able and willing to provide voluntary written/thumb-printed informed consent for the infant to participate in the study.*
6. *Infant's parent(s) or legal guardian must be willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures.*
7. *The infant's mother must provide related medical certificate(s) for the negative results for HIV, HBV and syphilis infection within 1 year prior to screening.*
8. *Infant's parent(s) or legal guardian must have a readily identifiable place of residence in the study area, be available for the duration of trial participation, and have a means of telephone contact.*

Note: For items with an asterisk (*), if the subject does not meet the criteria, the visit may be rescheduled when the criteria is met.

Kriteria Eksklusi / Exclusion criteria

1. *Use of any investigational product other than that used in the study prior to randomization or planned use of such a product during the period of study participation.*
2. *History of S. pneumoniae infection as confirmed by laboratory testing if available.*

3. *The infant who are children in care, preterm and low-birth-weight (Preterm infants have a gestational age below 37 weeks at birth and low birth-weight infants have a birth weight below 2.5 kg).*
4. *History of allergic disease or history of a serious reaction to any prior vaccination or known hypersensitivity to any component of the investigational vaccine, and/or all components of the hexavalent vaccine.*
5. *History of anaphylactic shock.*
6. *Any abnormal vital sign as judged by the investigator.*
7. **Participant experiences acute diseases or acute exacerbation of chronic diseases or uses antipyretic, analgesic and anti-allergic drugs (such as paracetamol, ibuprofen, aspirin, loratadine, cetirizine, etc.) within 3 days before vaccination.*
8. **History of administration of attenuated vaccines within 14 days (<14 days) and inactivated vaccines within 7 days (<7 days) prior to the 1st dose of investigational vaccine (If the participant[s] does not meet the criteria, the visit may be rescheduled when the criteria are met).*
9. *Previous vaccination against diphtheria, tetanus, pertussis, polio, hepatitis B, Haemophilus influenzae type b, Neisseria meningitidis and/or Streptococcus pneumoniae with the exception of vaccines where the first dose can be given before 2 months of life according to the national recommendations.*
10. *History of intercurrent diphtheria, tetanus, pertussis, hepatitis B, polio, Haemophilus influenzae type b disease, Neisseria meningitidis.*
11. *Individuals who receive treatment with radiotherapy or immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids (if systemic corticosteroids are administered for ≥ 14 days at a dose of ≥ 10 mg/day of prednisone or equivalent), e.g., for cancer or an autoimmune disease, or planned receipt throughout the study. Inhaled/nebulized, intra-articular, epidural, or topical (skin or eyes) corticosteroids within indicated dosage are permitted.*
12. **Administration of immunoglobulins and/or any blood products or anticipation of such administration within 28 days before vaccination and during the study period.*
13. *History of known disturbance of coagulation or blood disorder that could cause anemia or excess bleeding (e.g., thalassemia, coagulation factors deficiency, severe anemia at birth).*
14. *History of suspected primary immunodeficiency.*
15. *History of meningitis, seizures or any neurological disorder.*
16. *A family history of congenital or hereditary immunodeficiency.*
17. *The infant is a direct descendant (child or grandchild) of any person employed by the Sponsor, the CRO, the investigator, study site personnel.*
18. *Any medical or social condition that in the opinion of the investigator may compromise the well-being of the study participant, interfere with the study objectives, pose a risk to the study participant, or prevent the study participant from completing the study follow-up.*

Note: For items with an asterisk (*), if the participant meets these exclusion criteria, the visit may be rescheduled for a time when these criteria are not met.

11. *Endpoint* Uji Klinik : *Primary Endpoints:*
    - *Percentage of participants with serotype-specific IgG concentrations ≥ 0.35 µg/mL, measured 30 days after the booster dose of the investigational vaccine.*
    - *Geometric mean concentration (GMC) ratio of serotype-specific IgG responses 30 days after the booster dose of the investigational vaccine.*

    Secondary endpoints:
    - *Incidence, severity and duration of each solicited (local and systemic) AE within 7 days after each dose of the investigational vaccine in all participants*
    - *Incidence, severity, and causality of unsolicited AEs within 30 days after each dose of the investigational vaccine in all participants.*
    - *Incidence, severity, and causality of SAEs from 1st dose to 6 months after booster dose of the investigational vaccine.*
    - *Percentage of participants with serotype-specific IgG concentrations ≥0.35 µg/mL, measured 30 days after 2nd dose of the investigational vaccine.*
    - *GMC of serotype-specific IgG responses 30 days after 2nd dose of the investigational vaccine.*
    - *Percentage of participants with serotype-specific OPA titer ≥1:8 30 days after the 2nd dose, before the booster dose, and 30 days after the booster dose of the investigational vaccine in OPA subgroup.*
    - *Geometric mean titers (GMTs) of serotype-specific OPA responses 30 days after the 2nd dose, before the booster dose, and 30 days after the booster dose of the investigational vaccine in OPA subgroup.*
    - *Seroconversion rate (SCR) and GMC of anti-diphtheria toxoid and anti-tetanus toxoid IgG responses 30 days after the 2nd dose of the investigational vaccine.*
    - *SCR and GMC of anti-pertussis toxin (PT), filamentous hemagglutinin (FHA) IgG responses 30 days after the 2nd dose of the investigational vaccine with respect to baseline.*
    - *SCR and GMC of anti-Haemophilus influenzae type b (PRP) IgG responses 30 days after the 2nd dose of the investigational vaccine.*
    - *SCR and GMC of anti-Hepatitis B surface antigen (HBsAg) responses 30 days after the 2nd dose of the investigational vaccine.*
    - *SCR of anti-polio antibody 30 days after the 2nd dose of the investigational vaccine.*

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol yang diajukan yang didukung oleh tim ahli melalui rapat pada tanggal 6 Agustus 2024 dengan hasil sebagai berikut:

1. Pemilihan 3 dosis (2 primer+1 booster) vaksin yang digunakan dalam uji klinik ini mengikuti rekomendasi WHO (*Pneumococcal conjugate vaccines in infants and children under 5 years of age: WHO position paper – February 2019*), sehingga uji klinik ini memiliki justifikasi yang kuat untuk dapat dilaksanakan.
2. Desain uji klinik yang diajukan dapat diterima.
3. Vaksin memenuhi persyaratan mutu.

Keputusan

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik (PPUK) No. RG.01.06.32.321.10.2024.9045 tanggal 1 Oktober 2024