RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN TIFOID KONJUGAT VI-DT *PERSISTENCE AND LONG-TERM PROTECTION*
PRODUKSI PT. BIO FARMA

Informasi Umum

1. Uji klinik merupakan uji klinik fase II yang bertujuan untuk mengevaluasi persistensi antibodi 2 tahun setelah satu dosis pemberian Vi-DT pada subjek dewasa, remaja, anak – anak dan bayi yang diberikan pada studi sebelumnya (Typhoid 0218).
2. Subjek yang telah mengikuti uji klinik Typhoid 0218 merupakan kandidat subjek uji klinik Typhoid 0220 ini yang selanjutnya akan dibagi ke dalam dua kelompok:
   a. Kelompok studi observasional untuk subjek dewasa 19 – 40 tahun, remaja 12 – 18 tahun dan anak 2 – 11 tahun. Subjek akan dilakukan pemeriksaan fisik dan pengambilan sampel darah pada tahun ke-3, 4, dan 5 setelah dosis Vi-DT sebelumnya. Subjek tidak akan mendapatkan vaksin tambahan pada kelompok studi ini.
   b. Kelompok studi intervensional untuk subjek bayi 6 – 23 bulan. Subjek akan mendapatkan satu dosis obat uji Vaksin Tifoid Konjugat Vi-DT baik yang pada studi sebelumnya mendapatkan obat uji ataupun dan selanjutnya dilakukan pengamatan pada tahun ke-1, 2, dan 3.

Informasi Uji Klinik

1.	Judul Protokol	:	***Persistence and Long-Term Protection of Vi Antibodies Induced by Vi-DT Conjugate Vaccines in Indonesian Adults, Adolescent, Children, and Infants*** No. Protokol Typhoid 0220 versi 1.a, tanggal 15 September 2020
2.	Produk Uji	:	*Purified Vi capsular polysaccharide of Salmonella typhi 25 µg conjugated to diphtheria toxoid,* sediaan *injeksi, 1 dosis 0,5 mL, multidose vial 5 mL @ 3,1 mL (5 doses).* Vaksin diberikan 1 dosis (*booster)* secara intramuskular pada subjek kelompok studi intervensional untuk subjek bayi 6 - 23 bulan baik yang pada studi sebelumnya mendapatkan obat uji ataupun pembanding (Vaksin Poliomielitis *Inactivated*). Produksi: PT. Bio Farma.
3.	Center/ Peneliti	:	Departemen Ilmu Kesehatan Anak, Fakultas Kedokteran Universitas Indonesia, Jakarta / dr. Bernie Endyarni Medise, Sp.A(K), MPH *Field sites :* 1. Puskesmas Jatinegara, Jakarta Timur 2. Puskesmas Senen, Jakarta Pusat
4.	Sponsor	:	PT. Bio Farma (Persero)
5.	Persetujuan Etik	:	- Keterangan Lolos Kaji Etik Komite Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Indonesia – RSUPN Dr. Cipto Mangunkusumo No. KET-731/UN2.F1/ETIK/PPM.00.02/2020 tanggal 13 Juli 2020.

- Persetujuan Amandemen Protokol No. ND-1213/UN2.F1/ETIK/PPM.00.02/2020 tanggal 5 Oktober 2020

6. Desain Uji Klinik : 1. *Observational Study:*
   Subject aged 2-40 years when receiving the primary dose.
   2. *Interventional Study:*
   Subject aged 6-23 months when receiving the primary dose

7. Jumlah Subjek : *A total 580 who completed the phase II Vi-DT study (Typhoid 0218) will involved in the study.*

8. Tujuan Uji Klinik : ***Primary Objective***
To evaluate antibody persistence 2 years after vaccination with one dose of Vi-DT in in adults, adolescents, children and infants groups.
Secondary Objective
1. *To evaluate immunogenicity 1 month after a booster dose of Vi-DT in subject aged 6- 23 months when receiving the primary dose.*
2. *To assess the safety following booster vaccination in subject aged 6-23 months when receiving the primary dose.*
3. *To evaluate antibody persistence 3, 4 and 5 years after vaccination with one dose of Vi-DT in adults, adolescents, and children groups.*
4. *To evaluate antibody persistence 1, 2 and 3 years after booster vaccination in subject aged 6-23 months when receiving the primary dose.*
5. *Kinetics of Vi-specific IgG antibodies up to 5 years after vaccination.*

9. Kriteria Eligibilitas : ***Inclusion Criteria****:*
Observational Study
1. *Subject who completed the phase II Vi-DT study (Typhoid 0218)*
2. *Subjects/Parents have been informed properly regarding the study and signed the informed consent form.*

Interventional Study
1. *Healthy.*
2. *Subject who completed the phase II Vi-DT study (Typhoid 0218).*
3. *Subjects/Parents have been informed properly regarding the study and signed the informed consent form.*
4. *Subject/parents/legal guardians will commit to comply with the instructions of the investigator and the schedule of the trial.*

Exclusion Criteria*:*
Observational Study
History of uncontrolled coagulopathy or blood disorders contraindicating for phlebotomy.
Interventional Study
1. *Subject concomitantly enrolled or scheduled to be enrolled in another trial.*
2. *Evolving mild, moderate or severe illness, especially infectious diseases or fever (axillary temperature ≥ 37.5°C).*

3. *Known history of allergy to any component of the vaccines.*
4. *History of uncontrolled coagulopathy or blood disorders contraindicating intramuscular injection.*

Any abnormality or chronic disease which according to the investigator might be compromised by the vaccination and/or interfere with the assessment of the trial objectives.

10. *L*uaran Uji Klinik/ *Endpoint* :

Primary Evaluation Criteria

Main evaluation criteria is number and percentage of subjects with four fold increasing antibody 2 years after vaccination compare to baseline and Geometric Mean Titre (GMT) of anti-Vi IgG in all groups 2 years after vaccination

Parameter to be measured

1. *Number and percentage of subjects with four fold increasing antibody 2 years after vaccination should be described with 95% confidence interval (CI).*
2. *Geometric Mean Titre (GMT) of anti-Vi IgG in all groups 2 years after vaccination.*

Secondary Evaluation Criteria

1. *Immunogenicity:*
   - *Number and percentage of subject aged 6-23 months with seroconversion defined as ≥ 4- fold increase in antibody titer 28 days after booster dose compared to pre-booster dose.*
   - *Geometric Mean Titre (GMT) of anti-Vi IgG after booster dose in subject aged 6-23 months.*
   - *Number and percentage of adults, adolescents and children with seroconversion defined as ≥ 4-fold in antibody titer of anti-Vi IgG 3,4 and 5 years after vaccination compared to baseline.*
   - *Geometric Mean Titre (GMT) of anti-Vi IgG in adults, adolescents and children 3, 4 and 5 years after vaccination.*
   - *Number and percentage of subjects with seroconversion defined as ≥ 4-fold in antibody titer of anti-Vi IgG 1,2 and 3 years after booster vaccination compared to baseline (antibody titers before booster).*
   - *Geometric Mean Titre (GMT) of anti-Vi IgG subjects in 1, 2 and 3 years after booster vaccination compared to baseline (antibody titers before booster).*
2. *Safety in interventional study:*
   - *Number and percentage of subject with at least one adverse event, solicited or unsolicited, within 30 minutes, 72hours, 7 days and 28 days after booster dose.*
   - *Number and percentage of subjects with serious adverse event (SAE) from inclusion until 28 days after booster dose.*

Parameters to be measured

1. *Immunogenicity*

   GMT, percentage of subjects with four fold increasing anti-Vi IgG antibody 2 years after Vi-DT. Should be described per group with 95% confidence interval (CI).

2. *Safety in interventional study:*
    - *Local reactions and systemic events occurring within 30, 72 hours, 7 days and 28 days after vaccination subject interventional study.*
    - *Any Serious Adverse Events occurring 28 days after vaccination will be described*

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol uji klinik vaksin Vi-DT, dengan hasil sebagai berikut:

1. Hasil uji klinik Vaksin Tifoid fase 2 yang telah dilakukan sebelumnya (Typhoid 0218) terhadap 580 subjek subjek dewasa, remaja, anak – anak dan bayi menunjukkan bahwa vaksin aman dan dapat ditoleransi dengan baik. Khususnya pada subjek 6-23 bulan menunjukkan Vi-DT *immunogenic* (menunjukkan respon imun) berdasarkan pengamatan pada hari ke-28 setelah pemberian obat uji.
2. Desain uji klinik yang diajukan mengevaluasi persistensi dan perlindungan jangka panjang antibodi dari pemberian vaksin tifoid telah memadai.
3. 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.01.06.1.3.11.20.33 tanggal 10 November 2020.